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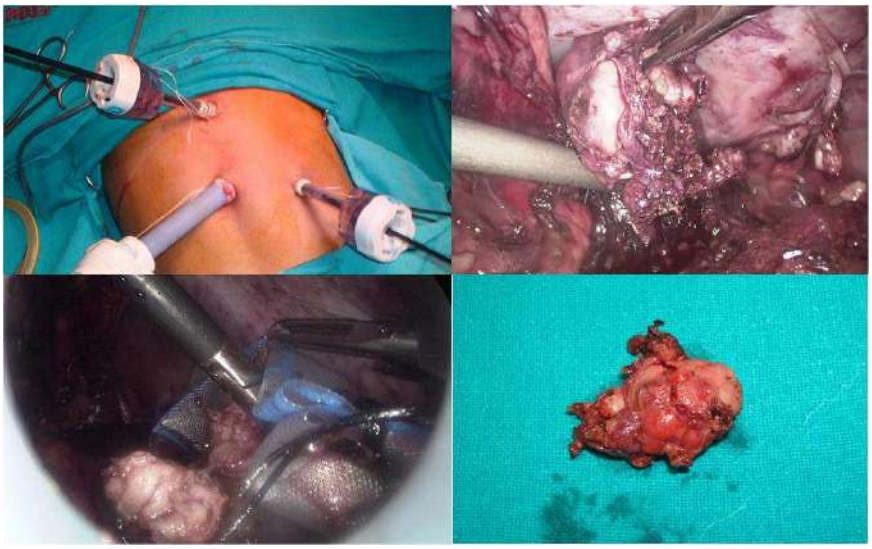
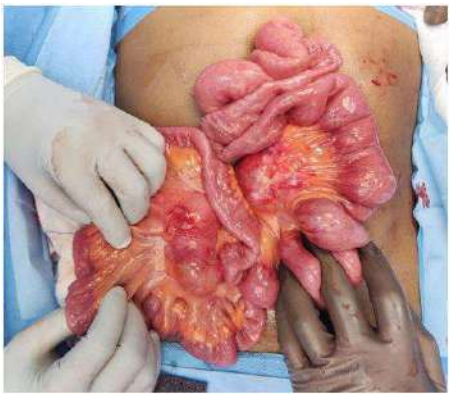
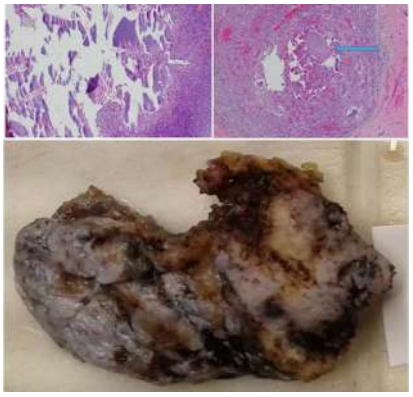


Laparoscopic surgical approach for pediatric intra-abdominal tumor (Neuroblastoma)



Intra-operative finding in 'Mesenteric Cyst'



Large granule of actinomyces, Suppurative inflammatory reaction (H&E, 20X), Eosinophilic Splendor-Hoeppli reaction (H& E, 10X) and Excised specimen.

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EDITORIAL

Health care reforms: Where do we stand among the other developing nations

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Improving population health is crucial for the development of a society, especially in some developing countries with vulnerable healthcare systems. In the past decade, there has been a growing recognition of the need for healthcare system reforms, particularly targeting the poor and disadvantaged groups who face financial barriers and are at risk of falling into the medical poverty trap. Empirical evidence and lessons from past experiences play a vital role in informing future health policy-making. By understanding what strategies and interventions have proven effective, policymakers can design and implement more efficient and equitable healthcare systems.

Some key areas where evidence-based interventions can contribute to better health policy-making includes, Universal health coverage, Primary healthcare strengthening, Health financing reforms, Health workforce planning and development, Health information systems and digital health.

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The out-of-pocket expenditure is the dominant source of health financing in India, as is the case in many other developing countries in the world [1]. In India, a significant portion of healthcare costs is paid directly by individuals at the point of service, leading to financial burden and potential barriers to accessing healthcare for many people.

The reliance on out-of-pocket expenditure can have several implications. Firstly, it can lead to financial hardship and push individuals and families into poverty, especially when faced with high healthcare costs. Secondly, it can create disparities in access to healthcare, as those with limited financial means may forego or delay seeking necessary medical treatment.

To address these challenges, the Indian government has taken various initiatives to expand health insurance coverage and reduce the reliance on out-of-pocket payments. For instance, the implementation of the Ayushman Bharat scheme, which includes the Pradhan Mantri Jan Arogya Yojana (PMJAY), aims to provide health insurance coverage to vulnerable and low-income populations. Through PMJAY, eligible individuals can access cashless hospitalization for specified medical conditions, thus reducing the financial burden (Figs. 1a, b and c).

Under the PMJAY, another scheme Pradhan Mantri Aarogya Mitra (PMAM) has been launched. The aim of this scheme is to create a cadre of certified frontline health service professionals who will be primary point of facilitation for the beneficiaries to avail treatment at the hospital and thus, act as a support system to streamline health service delivery (Fig. 2).

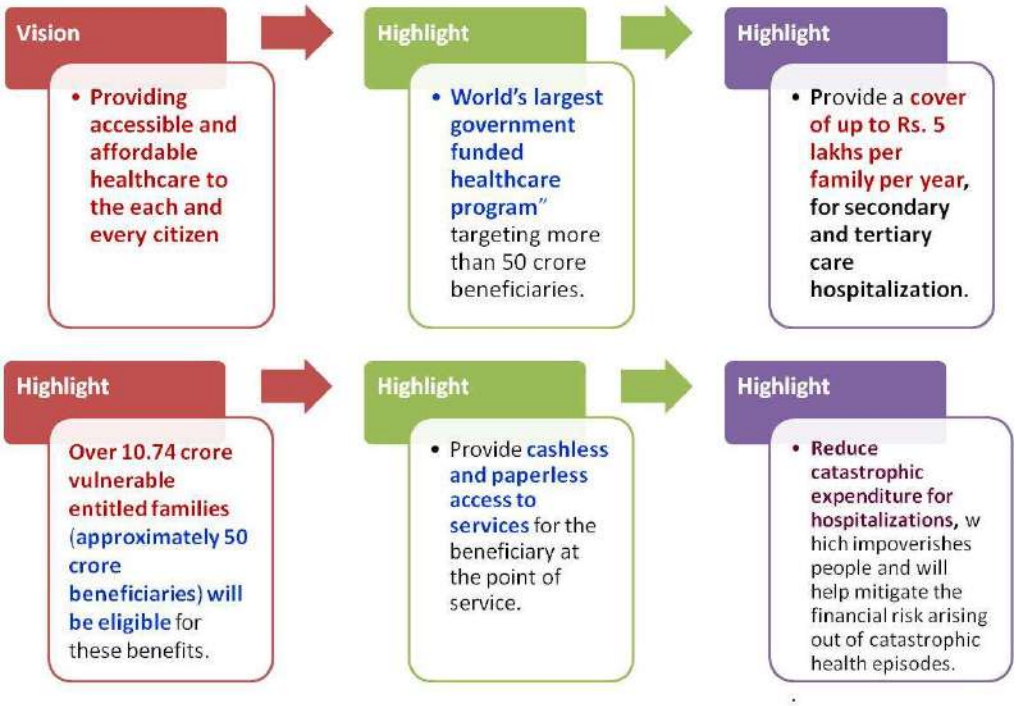

Fig. 1a. Highlights of Pradhan Mantri Jan Arogya Yojana (PMJAY)

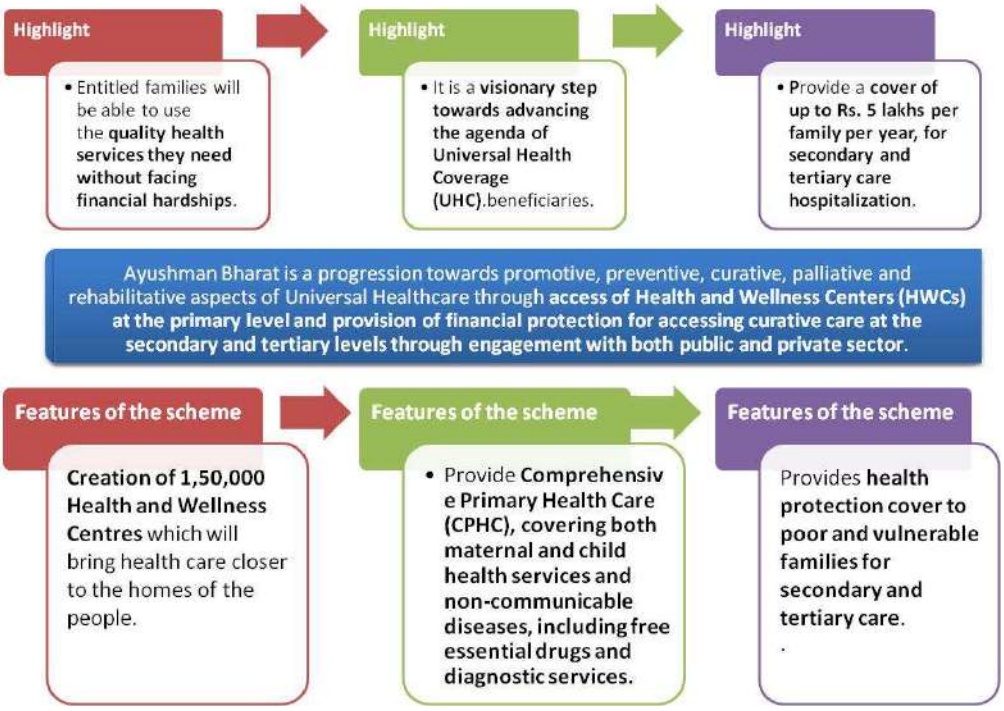

Fig. 1b. Highlights and Features of PMJAY

Fig. 1c. PMJAY: Financial protection from catastrophic expenditure

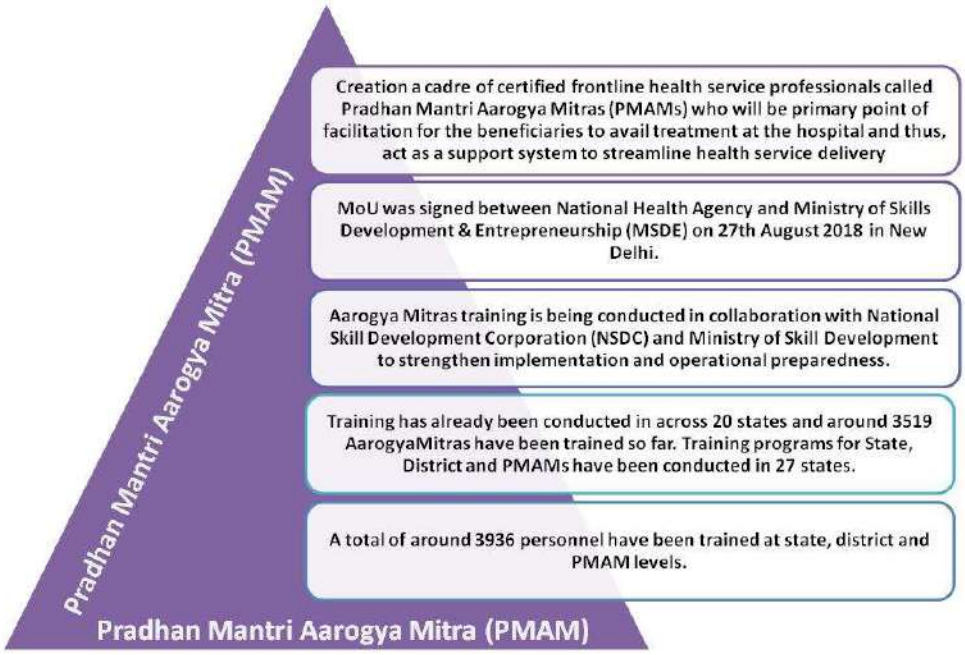

Fig. 2. Highlight and Features of Pradhan Mantri Aarogya Mitra (PMAM)

On the other hand, the government has been working towards strengthening primary healthcare and promoting affordable and accessible healthcare services. Initiatives like the establishment of more primary health centers, the availability of essential drugs at subsidized rates, and the expansion of free or low-cost healthcare services for specific groups aim to improve access and reduce the need for out-of-pocket expenditure.

Major challenges

Any healthcare system among the developing nations faces several challenges that impact its effectiveness and accessibility. Here are some of the key challenges such as accessibility to quality healthcare services particularly in rural and remote areas, maldistribution of healthcare facilities, shortage of healthcare professionals, inadequate access to essential healthcare services for a significant portion of the population. While efforts have been made to expand health insurance coverage, achieving universal coverage and reducing the reliance on out-of-pocket payments remains a challenge [2].

Uneven distribution of healthcare workforce between urban and rural areas risks exacerbation of access gap. Strengthening quality assurance mechanisms, enhancing healthcare provider accountability, and promoting standardized protocols are essential for improving the quality of care.

India faces a double burden of communicable and non-communicable diseases. Effective prevention, early detection, and management of these diseases are critical challenges. Adequate health information systems for data collection, analysis, and monitoring are vital for evidence-based decision-making and policy formulation.

The current focus of the Government is on strengthening healthcare infrastructure,

expanding access to quality care, enhancing healthcare financing mechanisms, investing in human resources for health, and improving the overall quality and efficiency of the healthcare system for addressing these challenges and improving healthcare delivery in India.

Health Reforms in India

The Indian government introduced the *National Health Policy in 2017* (Fig. 3) & *Pradhan Mantri Jan Arogya Yojana (PMJAY)* was launched in 2018. India faced a significant health challenge during the COVID-19 pandemic, as a result, the government implemented various measures, including expanding testing and healthcare infrastructure, launching vaccination campaigns, and providing financial support to affected individuals and businesses.

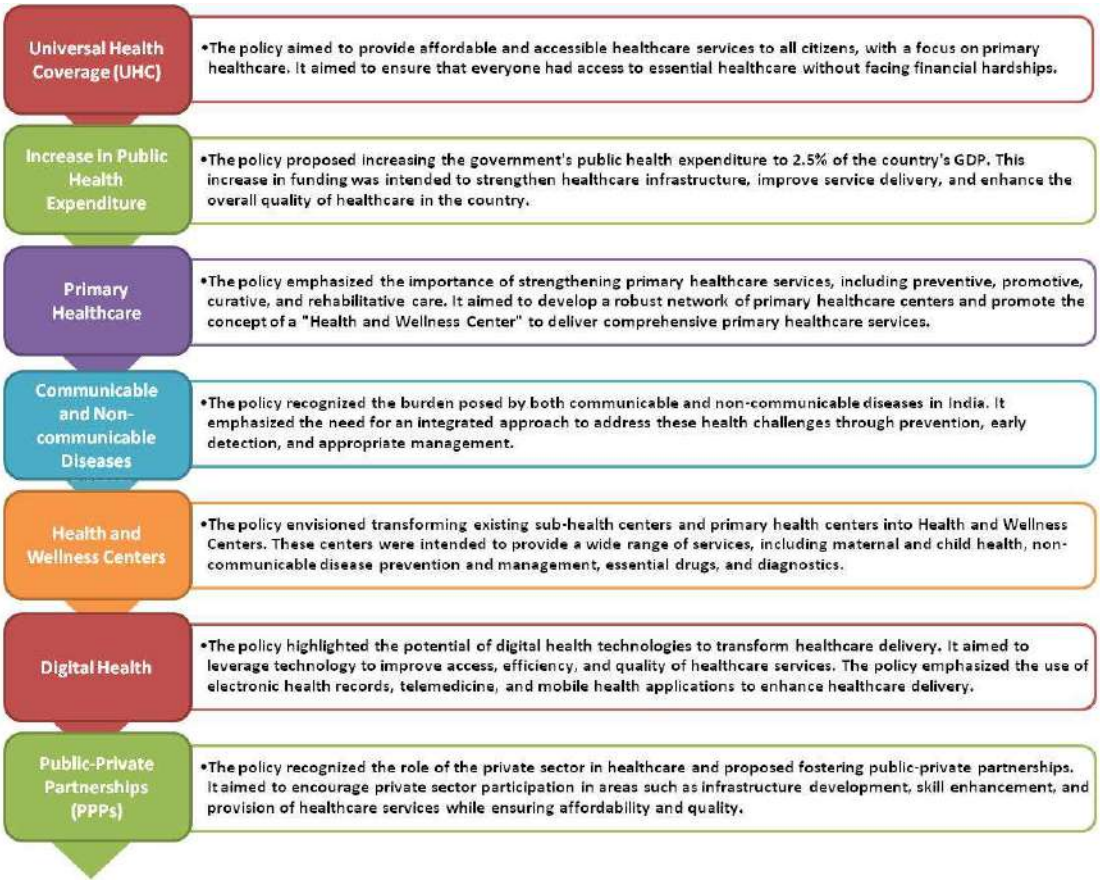

Fig. 3. Some key highlights of the National Health Policy 2017. The National Health Policy 2017 was a significant document that outlined the government's vision and strategies for healthcare in India.

Health Reforms in Other Developing Countries

Healthcare reforms vary across different developing countries. Here are a few examples of health reforms implemented in some countries during the mentioned period:

Brazil

The Brazilian government implemented the “Mais Médicos” (More Doctors) program in 2013, which aimed to improve access to healthcare services, especially in rural and underserved areas. The program recruited foreign and domestic doctors to work in areas with a shortage of healthcare professionals [3].

The "Mais Médicos" program emphasized primary healthcare services, focusing on preventive care, health promotion, and basic medical services. It aimed to address the broader healthcare needs of communities and improve overall health outcomes. In recent years, there have been modifications to the program, including changes to the participation requirements and increased emphasis on the integration of participating doctors into the Brazilian healthcare system.

South Africa

South Africa introduced the National Health Insurance (NHI) scheme to achieve universal health coverage. The NHI aims to provide affordable healthcare services to all South Africans, regardless of their socioeconomic status, by pooling funds and implementing a single-payer system [4].

It seeks to provide a comprehensive package of healthcare services, including primary healthcare, hospital care, and specialist services. The NHI proposes a single-payer system where healthcare services are funded through a compulsory prepayment system. The funding sources are expected to include general taxes, payroll taxes, and mandatory contributions. The NHI will be governed by a centralized agency responsible for purchasing and coordinating healthcare services. The NHI places emphasis on strengthening the district health system, which serves as the primary level of care delivery. This involves improving primary healthcare infrastructure, staffing, and service delivery at the local level. Under the NHI, the government will act as the single purchaser of healthcare services. The NHI implementation is planned to occur in phases over several years. Pilot projects and demonstration sites have been initiated to test and refine the proposed NHI models and strategies before nationwide scaling.

Mexico

Mexico implemented a series of health reforms, including the creation of Seguro Popular, a public health insurance program, in 2003. The program aimed to expand access to healthcare services for the uninsured population and reduce financial barriers to care [5].

The program offers a comprehensive package of healthcare services, including preventive care, primary healthcare, hospitalization, medications, surgeries, and treatments for a wide range of conditions. The benefits are designed to meet the basic healthcare needs of the insured population. Seguro Popular aims to protect individuals and families from high out-of-pocket healthcare expenses. The program operates on a contributory basis, where individuals and families contribute to the insurance premium based on their income level. It establishes partnerships with public and private healthcare providers to ensure access to a network of healthcare facilities. Since its inception, Seguro Popular has undergone

various expansions and improvements to enhance coverage and service delivery.

In recent years, the Mexican government has undertaken healthcare reforms to transition from Seguro Popular to a new healthcare model called the Instituto de Salud para el Bienestar (INSABI), which aims to further improve healthcare access and quality for the population.

China

China has implemented several healthcare reforms to address issues related to accessibility, affordability, and quality of care [6].

In 2009, China launched a comprehensive healthcare reform plan to improve its healthcare system. The reforms aimed to strengthen primary healthcare services, expand health insurance coverage, and enhance the quality and accessibility of healthcare services across the country. The government has expanded the coverage of the basic medical insurance system, including the Urban Employee Basic Medical Insurance (UEBMI) and the New Rural Cooperative Medical Scheme (NRCMS). These programs provide health insurance to urban employees and rural residents, respectively, and aim to reduce financial barriers to healthcare. China has focused on strengthening primary healthcare services to improve accessibility and ensure that individuals receive appropriate care at the community level. They have embraced digital health technologies to enhance healthcare delivery. This includes the implementation of electronic health records, telemedicine services, and mobile health applications.

It's important to note that the Chinese healthcare system is vast and complex, with variations in healthcare delivery across different regions.

Vietnam

The healthcare system reform in Vietnam has focused on the promotion of social health insurance as a means to address the dominant reliance on out-of-pocket expenditure. Some key points regarding the social health insurance system in Vietnam have been mentioned below [7].

Vietnam established a compulsory social health insurance program called the Health Care Fund for the Poor (HCFP) in 1992. The program targets poor households and selected disadvantaged groups, such as people of merit, the elderly, and war dioxin victims. Eligible individuals for the HCFP are determined based on existing government program lists and household surveys. However, self-employed workers, informal sector workers, and dependents of Comprehensive Health Insurance (CHI) members are not covered under this program. The HCFP is funded entirely by public finance, with contributions from the central and provincial governments. The program adopts a fee-for-service payment method for both outpatient and inpatient care. This payment approach may lead to supply-induced demand for healthcare, potentially resulting in over-treatment by physicians.

Vietnam Social Security (VSS): In 2003, Vietnam Social Security (VSS) was established to administer all social insurance programs, including collecting premiums, issuing health insurance cards, and reimbursing service providers. While the

social health insurance system in Vietnam has expanded coverage and improved access to healthcare services, challenges such as limited financial resources, regional disparities, and issues related to fee-for-service payment methods remain.

Health reforms variation among the countries

The extent and nature of health reforms can vary widely across countries, depending on their specific contexts, healthcare systems, and policy priorities.

The concerns regarding policy design in healthcare reforms

Differences in social development, poverty levels, and population health among regions or target populations can significantly influence the outcomes of healthcare reforms. Addressing these disparities requires tailored policies and interventions to meet the specific needs of different populations. The design of healthcare system reforms plays a crucial role in determining their effectiveness. This includes interventions on both the demand side (such as health insurance coverage and access to care) and the supply side (such as healthcare infrastructure and workforce capacity).

Regular evaluation and monitoring of the reform's progress can help identify and address any shortcomings or implementation gaps. The selection of the target population and the design of the benefit package under social health insurance reforms are critical considerations.

Taking into account the unique context, population needs, and healthcare system dynamics can lead to more effective and sustainable reforms that address issues of accessibility, affordability, and quality of care [8].

The background differences across countries, such as social development, poverty level, and population health, play a significant role in shaping policy differences and outcomes. Importing policies from other countries without accounting for these differences may lead to unexpected or suboptimal outcomes. Tailoring policies to address the unique challenges and needs of each country is crucial for achieving desired results in healthcare reforms.

Conflicts of interest

The authors declares that they do not have conflict of interest.

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ORIGINAL ARTICLE

Laparoscopic abdominal tumor resection: Further evidence for expanding on the current SIOP criteria based upon a Single Centre, Single Surgeon series of 28 children

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Abstract

Purpose: The purpose of the study was to evaluate the safety and feasibility of laparoscopic resection in paediatric patients with abdominal tumors. This is a retrospective observational study that focuses on a specific population of patients who underwent laparoscopic surgery for intra-abdominal solid malignancies in the department of paediatric surgery, All India Institute of Medical Sciences, New Delhi 110029, India. The results could help guide healthcare professionals in making informed decisions regarding the use of minimally invasive surgery (MIS) for diagnosing and treating abdominal tumors in children.

Methods: Total 28 children presenting with paediatric intra-abdominal tumors were included in which wilm's tumor (*n*=20), ganglioneuroblastoma (*n*=1) neuroblastoma (*n*=2), adrenal cortical tumor (*n*=2), ovarian tumor (*n*=2) and one patient had bilateral pheochromocytoma (*n*=1). Children were between 10 months-14 years (mean 46.6 months). A 3 or 4 port laparoscopic procedures were performed and lymph node sampling was carried out.

Results: The results of the study showed successful removal of the tumors in all cases, except for one instance of rupture. Specimens were retrieved through either a lumbar incision (*n*: 26 cases) or a Pfannenstiel incision (*n*: 2 cases). There were no conversions to open surgery. All the children underwent regular follow-up.

Conclusion: A laparoscopy or laparoscopic-assisted removal of paediatric intra-abdominal tumors is a safe and feasible option. This approach offers advantages such as reduced postoperative pain, shorter hospital stay, and better cosmetic results. The authors emphasized the importance of proper patient selection, appropriate port placement, and the surgeon's experience in laparoscopic techniques as contributing factors to successful outcomes. This report also provides further evidence to expand on the current SIOP criteria & support MIS in treatment protocols for tumors.

Key words: Laparoscopy; wilms; neuroblastoma; adrenal tumor; phaeochromocystoma; solid tumors; children; SIOP criteria

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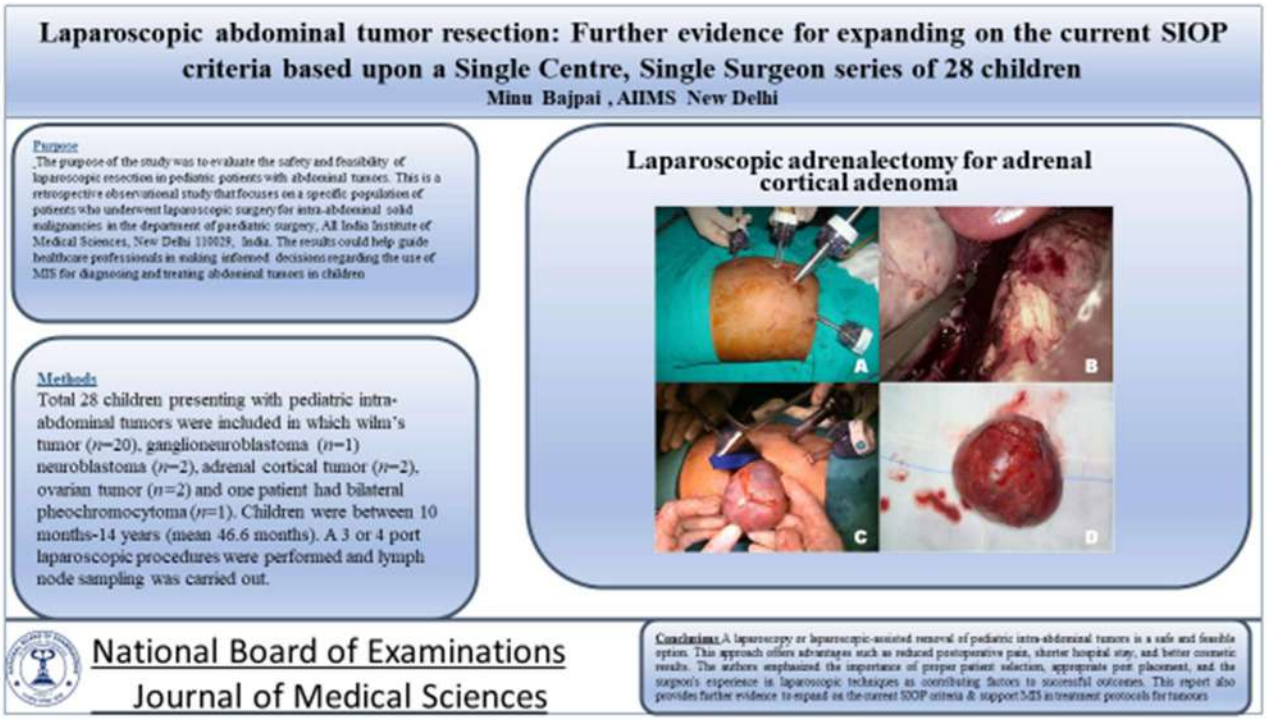
Graphical Abstract



Introduction

It is important to note that due to limited cancer registries and under-reporting in certain regions, the incidence of paediatric abdominal tumors in India may be underestimated. However, there are ongoing efforts to improve cancer surveillance and reporting in the country, which may lead to more accurate incidence estimates in the future. The paediatric abdominal tumors present diagnostic and technical challenges. Obtaining adequate tissue for diagnosis and treatment planning is crucial in these cases. Multiple diagnostic modalities, such as histologic, karyotypic, and molecular analyses, may be necessary to accurately diagnose these tumors. In certain situations, imaging studies may indicate that a tumor is unresectable at the time of diagnosis. However, obtaining a tissue sample for further analysis becomes essential in such cases. This is where laparoscopy, a minimally invasive surgical technique, can be beneficial in children with intraabdominal tumors.

Laparoscopy allows for a more precise visualization and access to the tumor site. It provides an opportunity to assess the tumor's size, location, and involvement with surrounding structures more accurately. The procedure involves making small incisions through laparoscope and other specialized surgical instruments are inserted into the abdomen. Compared to traditional open surgeries, laparoscopic procedures generally result in less post-operative pain, scarring, and shorter recovery times. These advantages are particularly important in paediatric patients, as it can minimize the physical and emotional stress associated with surgery.

Methodology

This is a retrospective observational study that focuses on a specific population of patients who underwent laparoscopic surgery for intra-abdominal solid malignancies during a certain period of time in the department of paediatric surgery at our institute. The study design involves reviewing past medical records and analyzing data to draw conclusions about the characteristics and outcomes of the patients.

One notable exclusion criterion in our study is patients who were not willing to participate. This exclusion could potentially introduce selection bias, as patients who declined to participate may have had different characteristics or outcomes compared to those who agreed to participate. It is important to note that retrospective studies are prone to several biases, and this should be taken into account when interpreting the results.

The established principles of oncology in the treatment of patients with solid intra-abdominal malignancies have been used. These principles involved a multidisciplinary approach to patient care, including the use of chemotherapy, imaging, and radiotherapy as per nationally accepted guidelines. A pre-operative ultrasound doppler was performed to assess for inferior vena cava (IVC) thrombus and involvement of adjacent organs. This non-invasive pathology test is an important part of the diagnostic workup for intra-abdominal malignancies, as it can help guide treatment decisions and surgical planning.

For instances that weren't invasive and didn't have an IVC thrombus or a distant metastasis, a laparoscopy was scheduled: All of the children were operated on by a single senior surgeon (MB), which could help ensure consistency in the surgical approach and potentially reduce variability in the outcomes. The study utilized a retrospective design, in which the admission records and follow-up files of the patients were assessed to gather data on the preoperative and post-operative characteristics of the patients. The use of retrospective data has advantages and disadvantages, as discussed earlier, but it can be a valuable way to analyze large amounts of information from past patient populations.

To ensure that the study was conducted in an ethical manner, parental consents were obtained, indicating that the parents of the children were made aware of the study and gave their permission for their child's medical records to be used. Additionally, we received an ethical waiver from the Institute's ethical committee, ensures that the committee reviewed the study proposal and determined that it posed minimal risks to patient confidentiality and privacy.

A laparoscopic procedure was performed under general anesthesia with the patient in a supine position, secured to the operating table with strapping. This allowed the surgeon to turn the tumor to optimal positions using gravity, which facilitated access to critical areas and reduced the risk of tumor rupture.

The laparoscopic excision of the tumor was performed using a three to four-port technique, which is a standard approach for laparoscopic surgeries. The technique was performed following the ergonomics of laparoscopy, which is important to reduce the risk of injury to the surgeon and the patient.

Tumor retrieval was performed through a near anatomical site incision, which is a common approach in laparoscopic surgeries. Lymph node sampling was performed under direct vision from a lumbotomy incision in cases of Wilms tumor and neuroblastoma. In addition, omental biopsy was taken in ovarian tumors if required. No drains were placed, and specimens were sent for histopathology examination. This is in line with the standard practice for laparoscopic surgeries, which typically do not require the use of drains or operative site washes. Post-operative pain was managed using intravenous or oral analgesics.

The demographic information of patient population included in the study

Total 28 children (17-males, 11-females) who presented to us with paediatric intraabdominal tumors were included. The tumors included Wilms tumor (n = 20), ganglioneuroblastoma (n = 1) neuroblastoma (n = 2), adrenal cortical tumor (n = 2), ovarian tumor (n = 2), bilateral pheochromocytoma (n = 1). Children were between 10 months–14 years (mean 46.6 months). A 3 or 4 port laparoscopic nephrectomy and lymph node sampling for Wilms tumor; adrenalectomy for adrenal tumors; and oophorectomy for ovarian tumor were performed. The case-wise distribution of the patients is presented in Table 1, which provides additional information about the types and locations of the tumors that were excised (Table 1).

Technique

Laparoscopic surgical procedures were performed under general anesthesia. The patients have been placed in the supine position, which means lying on their back. The patients were strapped to the operating table to ensure stability during the procedure. By using gravity, the tumors were turned to optimal positions, to improve access to critical areas without the need for excessive physical force. This approach also helps to avoid the risk of tumor rupture. A 3 to 4-port technique of laparoscopy have been employed for tumor excision. The ergonomics of laparoscopy have been followed to ensure optimal positioning and comfort for the surgical team. The tumors were retrieved through a small incision near the anatomical site where the tumors were located. In cases of Wilms tumor and neuroblastoma, lymph node sampling was performed. This has been done under direct vision from a lumbotomy incision, which is an incision made in the lower back area [1]. An omental biopsy have been taken in cases involving ovarian tumors. No drains were placed, as we did not deem it necessary to insert drainage tubes after the procedure. The excised tumors and other relevant tissues have been sent for histopathology examination to determine the nature and characteristics of the tissues. No washes have been given at the operative site. No additional cleaning or irrigation has been performed at the surgical site after the procedure. Pain after the surgeries has been managed using intravenous and oral analgesics.

With the exception of one, none of the tumors ruptured during removal. Through lumbar incisions (n = 20) and Pfanninsteil incisions (n = 8), specimens were removed. Open surgery was not performed in any cases. All of the kids are regularly monitored. Local recurrence of a Wilms tumor occurred

in one child. One child needed a port tract excision due to a port-site recurrence. One had open surgery for recurrence after neuroblastoma in a youngster. There were no deaths in this study group.

Table 1. Distribution of cases

S. No.	Histological Diagnosis	Age at Surgery (Months)	Gender	Site (Left, Right or Bilateral)	Stage	Pre-operative Chemotherapy	Pre-operative Tumor Volume (cm^3)	Complication
1.	Wilm's Tumor	52	Male	Left	III	Yes	1500	No
2.	Wilm's Tumor	24	Male	Right	III	Yes	528	No
3.	Wilm's Tumor	28	Female	Left	III	Yes	1170	No
4.	Wilm's Tumor	10	Female	Left	III	Yes	432	No
5.	Wilm's Tumor	31	Male	Left	III	Yes	1560	No
6.	Wilm's Tumor	68	Male	Right	III	Yes	936	No
7.	Wilm's Tumor	33	Male	Right	III	Yes	1040	Port site recurrence
8.	Wilm's Tumor	41	Female	Left	III	Yes	1320	No
9.	Wilm's Tumor	36	Male	Right	III	Yes	1040	No
10.	Wilm's Tumor	48	Male	Left	III	Yes	640	No
11.	Wilm's Tumor	27	Male	Left	III	Yes	1320	Pre-rupture and post-operative recurrence
12.	Wilm's Tumor	21	Female	Right	III	Yes	960	No
13.	Wilm's Tumor	32	Male	Left	III	Yes	1440	No
14.	Wilm's Tumor	33	Female	Right	III	Yes	1160	No
15. *	Wilm's Tumor	60	Male	Left	III		1560	Port-site recurrence
16.	Wilm's Tumor	24	Male	Left	III	Yes	1140	No
17.	Wilm's Tumor	41	Female	Right	III	Yes	1070	No
18.	Wilm's Tumor	27	Male	Left	III	Yes	970	Surgical site infection
19.	Wilm's Tumor	48	Male	Left	III	Yes	1090	No
20.	Wilm's Tumor	45	Male	Right	III	Yes	1120	No
21.	Ganglioneuroblastoma	36	Male	Right	II	Yes	384	No
22.	Neuroblastoma	40	Female		II	Yes	294	No
23.	Neuroblastoma	44	Male	Right	II	Yes	315	Local recurrence
24.	Immature ovarian teratoma	64	Female	Right	N/A	No	792	No
25.	Yolk sac ovarian tumor	170	Female	Left	I	Yes	792	No
26.	Adrenal cortical carcinoma	36	Male	Right	II	No	120	No
27.	Adrenal cortical adenoma	42	Female	Right	II	No	200	No
28.	Pheochromocytoma	144	Female	Bilateral	II	No	100/120	No

* WAGR syndrome: Wilms tumor, aniridia, genitourinary anomalies, mental retardation syndrome.

All patients with Wilms tumor, neuroblastoma, and ovarian tumor received pre-operative chemotherapy to shrink the size of the tumors and better define the margins of the lesions, which could make them easier to remove during surgery. The patients were selected on the basis specific criteria. Specifically, all cases were resectable on cross-sectional imaging with a well-defined plane of dissection and no inferior vena cava (IVC) thrombus or distant metastasis. This means that the tumors were deemed to be operable and able to be removed through laparoscopic excision. Before the laparoscopic procedure, the parents underwent a thorough consultation with the anesthesia team to ensure that they were fit for surgery and to plan the anesthesia approach that would be used during the laparoscopic procedure. These patients were initially considered non-resectable due to the large size of the tumor at presentation and were given chemotherapy before surgery. They were classified as having NWTS tumor stage–I (n = 1), stage–II (n = 3) and stage–III (n = 23) and no staging in 1 patient. The patients with neuroblastoma had right-sided tumors and were classified as having INRG-SS L2 stage. They received chemotherapy and were operated on after 18 weeks of treatment.

Adrenal cortical adenoma is a benign tumor of the adrenal gland that produces excess hormones, while adrenocortical carcinoma is a malignant tumor that can also produce excess hormones. In the case series, the adrenal cortical adenoma was detected incidentally for unrelated abdominal pain, while the adrenocortical carcinoma presented with excessive hair growth and hoarse cry. No chemotherapy was given for these tumors, and they were operated on at 42 and 36 months of age, respectively. The patient with bilateral pheochromocytoma had her blood pressure well-controlled with alpha-blockers and beta-blockers in the pre-operative period. Pheochromocytomas are rare tumors that secrete catecholamines, which can cause episodes of hypertension, sweating, and palpitations. It's important to control blood pressure prior to surgery, as manipulation of the tumor during surgery can cause sudden release of catecholamines leading to hypertensive crisis. The use of alpha-blockers and beta-blockers is the standard treatment for such cases. The pre-operative imaging determine the size and location of the tumors. In the situations of Wilms tumor and neuroblastoma, pre-operative cytology has been used to make a diagnosis. However, for ovarian and other adrenal tumors there was no pre-operative tissue collection done (Table 1).

The Pfannenstiel incision was used for ovarian tumors, which is a common approach for gynecologic surgeries. It has been assured that there was minimal intraoperative blood loss and no need for blood transfusion. The tumor retrieval bagsfor pheochromocytoma and adrenal cortical tumors has been used to prevent the spread of potentially malignant cells during the surgery.

Lymph node sampling has been done as it is an important aspect of the surgical management of many malignancies, as it helps to determine the extent of disease and guide further treatment decisions. In our case series, the extended lumbotomy incision has been utilized to provide good exposure to the

tumor bed and enable lymph node sampling. This approach was successful in all cases of Wilms tumor and one case of neuroblastoma, with a range of 3 to 7 lymph nodes retrieved. Additionally, in one case of ovarian tumor, omental biopsy was required due to dense adhesion of the ovarian mass to the omentum. This highlights the importance of thorough intraoperative assessment and the potential need for additional procedures to ensure complete resection of the tumor and accurate staging.

The patients with Wilm's and neurblastoma tumor were positioned in a supine position with a roll placed beneath the affected side to elevate the patients by up to 20 degrees. The patients were securely strapped to the operation table. Different table-tilting positions could be safely achieved during the procedure, which were particularly helpful in dissecting very large tumors.

The surgical technique used a standard three- to four-port approach for tumor resection. A 12mm camera port and 12 or 5mm working ports were used. The camera port was consistently inserted through the umbilicus in all cases.

The initial assessment of the tumor confirmed its extent and verified that it did not infiltrate nearby structures. To expose the tumor limits, either the right or left colon was displaced medially. Dissections were performed using a Harmonic scalpel or an electrocautery hook. A blunt metallic suction cannulas were used to lift the tumor and create a fulcrum against the posterior abdominal wall. This maneuver helped improve accessibility and control of the hilar vessels, especially in cases where the tumor overhung and obstructed the hilum.

The tumors were dissected along all its borders using the Harmonic scalpel, and vascular clips were applied for closure of the hilar vessels before division. The specimens were secured in a retrieval bag, and both specimen retrieval and lymph node sampling were performed through an extended lumbotomy incision. Typically, a lumbotomy incision is made transversely, 1 cm below the 12th rib, starting from the medial edge of the erector spinae and extending laterally by 4–5 cm. However, for larger tumors, these incisions were extended anteriorly by a few additional centimeters, creating an extended lumbotomy incision. Figures 1–3 accompany the text to provide visual representations of the described techniques and incision sites.

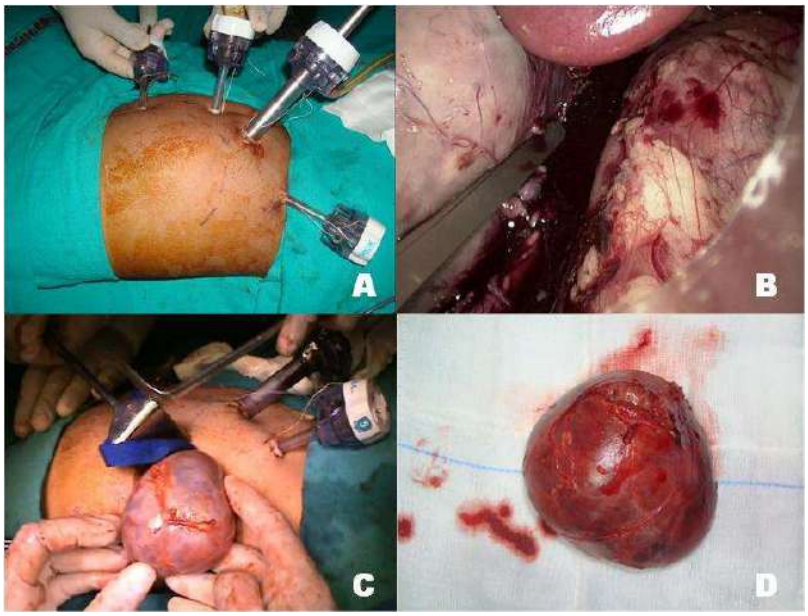


Figure 1 **(A-D)**. Laparoscopic adrenalectomy for adrenal cortical adenoma. **A.** Port placement; **B.** Intraoperative; **C.** Lumboscopic incision; **D.** Tumor

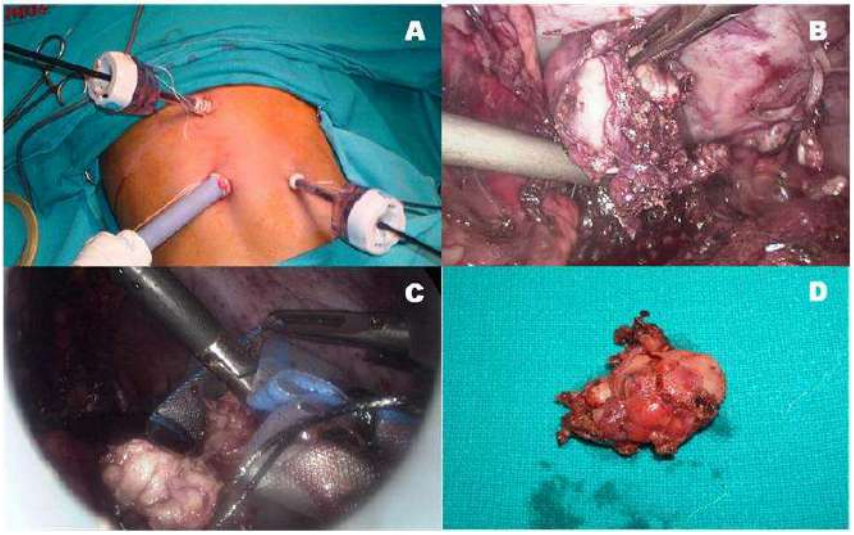


Figure 2. (**A-D**). Laparascopic approach for neuroblastoma. **A.** Port placement; **B.** Intraoprative; **C.** Tumor retrieval; **D.** Tumor

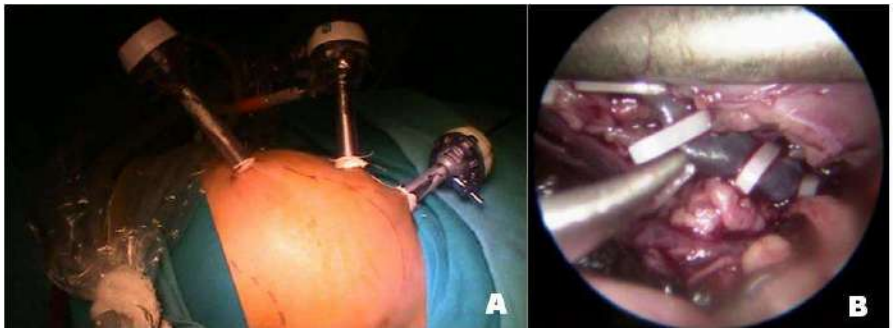


Figure 3. (**A-B**). Laparoscopic nephrectomy for Wilms tumor. **A.** Port placement; **B.** Vascular clipping.

Our patients have been provided with oral intake shortly after surgery and that post-operative chemotherapy was started before discharge and continued according to the protocol. The mean hospital stay of 5.6 ± 1.6 post-operative days is also a positive outcome. The patient with pre-operative tumor rupture experienced a recurrence after surgery despite receiving radiotherapy and chemotherapy. It is important to closely monitor and manage such cases with advanced chemotherapy. Similarly, the case of neuroblastoma with local recurrence highlights the importance of close follow-up and early intervention in case of recurrence. Patient is doing well after the re-exploration surgery.

The immature ovarian teratoma, adrenal cortical tumors, and pheochromocytoma were successfully managed with surgery alone without the need for adjuvant therapy. However, it is concerning to hear about the cases of local recurrence, particularly in the patient with pre-operative tumor rupture and the case of neuroblastoma. It is important for these patients to receive appropriate management and follow-up to ensure the best possible outcome. The patients have been successfully treated and are being closely monitored for any potential recurrence or complications. Regular follow-up is crucial to ensure the ongoing health and well-being of these patients.

Discussion

Laparoscopic surgery, also known as minimally invasive surgery, involves making small incisions in the abdomen and inserting a thin, flexible tube with a camera and surgical instruments attached. This approach allows for less tissue trauma, shorter hospital stays, and faster recovery times compared to traditional open surgery. The use of laparoscopy in paediatric surgery began in the 1990s, and its use in the management of paediatric abdominal tumors has increased over the years. The first reported laparoscopic excision of a paediatric abdominal tumor was in 1991, when a 3-year-old boy underwent laparoscopic removal of a Wilms tumor [2].

Since then, several studies have reported the successful use of laparoscopy in the management of a variety of paediatric abdominal tumors, including neuroblastomas, hepatoblastomas, and ovarian tumors. In particular, laparoscopic surgery has become the preferred approach for the treatment of ovarian tumors in children, as it offers excellent visualization and allows for complete excision of the tumor while preserving ovarian function.

Benign mature ovarian teratoma is indeed the most common ovarian tumor in children and typically requires surgical management [3,4]. However, performing a unilateral oophorectomy (removal of one ovary) at a young age can potentially lead to a shorter reproductive life span and early onset of menopause [5]. To preserve future fertility, it has been recommended that ovarian sparing surgery (removal of the tumor while preserving the ovary) should be the primary surgical procedure for the treatment of benign ovarian tumors in children [6].

Laparoscopy provides a wider field of vision and enhanced magnification, which can help paediatric surgeons to mobilize and

dissect tumors with greater precision and minimal injury to adjacent structures. This can be especially important in the management of complex tumors or tumors that are located close to vital organs or blood vessels.

In addition, laparoscopic surgery can benefit from advanced energy sources such as the Harmonic scalpel and Ligasure, which can help to release adhesions and provide better control of intraoperative bleeding. These tools use advanced energy technology to cut and coagulate tissue, minimizing bleeding and tissue trauma and facilitating faster and safer surgical procedures. Neoadjuvant chemotherapy has been shown to be effective in reducing the size of paediatric abdominal tumors and forming a pseudo-capsule, which can make the tumor more amenable to resection and minimize the risk of rupture during surgery. Many studies have supported the use of neoadjuvant chemotherapy in the management of paediatric abdominal tumors, including Wilms tumor.

While there have been some case reports suggesting the feasibility of laparoscopic nephrectomy as an upfront surgery for Wilms tumor and cases with lung and peritoneal metastasis [7,8]. We not currently promote minimally invasive surgery (MIS) for upfront laparoscopic surgery in such cases. However, we anticipate that laparoscopy may play a role in the management of advanced and metastatic disease in the future. The selection of surgical approach and treatment plan should be individualized based on the specific characteristics of each patient's tumor and overall health status, and should be made in consultation with a multidisciplinary team of paediatric oncologists, surgeons, and other specialists.

The laparoscopy can be a valuable tool in the management of large and advanced-stage paediatric abdominal tumors. In some cases, the size of the tumor may initially seem like a limitation for laparoscopic resection, but in practice, laparoscopy can often provide excellent access to the tumor and surrounding structures, allowing for selective dissection and ligation of the hilar vessels.

In our patients, pre-operative chemotherapy helps to reduce the size of the tumor and make it more amenable to laparoscopic resection. However, even in cases where the tumor remains bulky after chemotherapy, laparoscopy still is a useful approach, particularly when combined with advanced energy sources and other surgical techniques.

In any case, it is essential to follow oncologic principles during laparoscopic resection of paediatric abdominal tumors, including complete tumor resection and lymph node sampling. With careful planning and execution, laparoscopy can provide a safe and effective alternative to open surgical approaches, with the added benefits of reduced morbidity and faster recovery for young patients. A laparotomy scar can be a visible reminder of a patient's disease, and in some cases, laparoscopy provides a more cosmetically acceptable alternative. In the case of paediatric abdominal tumors, laparoscopy may be particularly useful for minimizing visible scarring in young patients who are still developing body image and self-esteem. For tumor retrieval during

laparoscopic procedures, there are several different approaches that can be used, including Pfannenstiel and umbilical incisions. However, the use of an incision close to the tumor bed may be preferred in some cases, particularly for renal and adrenal tumors. In this series, we have reported using a lumbotomy incision for tumor retrieval in most cases, while reserving a muscle-splitting Pfannenstiel incision for ovarian masses.

The choice of incision site and approach should be tailored to the specific characteristics of each patient's tumor and the overall goals of the procedure. In some cases, the use of multiple incisions may be necessary to provide optimal access and visualization during laparoscopic resection. The extended lumbotomy incision appears to offer several advantages over the classical transverse abdominal incision and the Pfannenstiel incision for paediatric abdominal tumor resection. One advantage is the limited size of the incision, which reduces the risk of complications and allows for quicker recovery. Additionally, the direct inspection of the tumor bed and tactile assessment can facilitate more precise and complete tumor resection.

Another advantage of the extended lumbotomy incision is the ability to perform berry picking of the lymph nodes. This technique involves identifying and removing lymph nodes that are directly adjacent to the tumor, which can help to prevent the spread of cancer cells and improve overall oncologic outcomes.

The posterolateral position of the scar also offers a psychological advantage by reducing the visibility of the scar and potentially alleviating anxiety in young patients. Moreover, taking out the tumor through the ipsilateral lumbotomy incision is safer than the distant Pfannensteil incision, as it reduces the risk of tumor seeding throughout the abdominal cavity.

Finally, the use of the extended lumbotomy incision can help to ensure that lymph node sampling is performed in accordance with oncologic principles. In contrast, the classical use of the Pfannenstiel incision can lead to a complete loss of pneumoperitoneum after specimen retrieval, limiting the ability to perform lymph node sampling for upper abdominal tumors and compromising oncologic outcomes. The extended lumbotomy incision provides several advantages, including direct inspection of the tumor bed with its tactile assessment, berry picking of the lymph nodes, and minimizing tumor seeding. Additionally, it allows for the retrieval of the tumor through an incision close to the tumor bed, reducing the risk of tumor seeding in the entire abdominal cavity. This approach also facilitates lymph node sampling from the tumor bed under direct vision, even after the loss of pneumoperitoneum, thus optimizing oncologic principles. Furthermore, the use of an ipsilateral lumbotomy incision confines the incision for tumor removal to the vicinity of the tumor and optimizes the field of radiation, if the same therapy is required, whereas a Pfannensteil incision would have required extended radiotherapy to a more distant region or whole abdomen radiation.

It is important to note that the incidence of port site recurrence after laparoscopic surgery in paediatric tumors is still not well-documented due to limited

follow-up literature. However, studies in adults with urothelial cancers have reported a low incidence of port site recurrence at 0.12% [9]. In the present case series, we have reported one case of port site recurrence which was managed successfully by excision of the port tract without any further recurrence. Nonetheless, it is important to closely monitor patients for any signs of recurrence or complications following laparoscopic surgery. The use of laparoscopy in neuroblastoma cases may be more limited in our setup due to the late presentation of cases, and the concerns regarding ovarian tumors have been addressed by limiting the use of MIS to smaller tumors and performing ovarian sparing procedures when possible. The MIS has also been explored for nephron sparing renal surgery, hepatic resection, pancreatic tumors, and sacrococcygeal masses, and that single-port surgeries and robotics may be future prospects in paediatric malignancies [10].

The optimal approach to tumor resection in paediatric malignancies is still a matter of debate and may vary depending on several factors, including the type, stage, and location of the tumor, as well as the surgeon's experience and preference. While laparoscopic approaches have been shown to offer certain advantages over open surgery, such as less pain, shorter hospital stays, and quicker recovery times, they may not always be feasible or appropriate in certain cases. As for the Cochrane review mentioned, it is important to keep in mind that the results of meta-analyses and systematic reviews may be limited by the quality and heterogeneity of the included studies, as well as other biases and confounding factors. Therefore, it is difficult to draw definitive conclusions about the comparative effectiveness and safety of different surgical approaches based on these types of reviews alone [11].

Lymph node sampling can be feasible with near-anatomical site incision approach. It's important to ensure adequate lymph node sampling for accurate staging and management of solid tumors. The role of MIS in paediatric malignancies is still a topic of debate and further research is needed to determine its safety and efficacy compared to traditional open surgery. While there are some reports of successful laparoscopic resections in certain cases, such as neuroblastoma and ovarian tumors with small diameter, concerns regarding the risk of incomplete resection and inadequate lymph node sampling still exist. However, with the development of newer technologies such as single-port surgeries and robotics, there may be potential for future implementation of MIS in paediatric malignancies [12].

Laparoscopy in paediatric solid tumors: Further evidence on a successful technique

An increasing number of paediatric cancer patients are undergoing minimally invasive surgery [13]. It is used for laparoscopic biopsies, tumor extent diagnosis, second opinions, as well as the total removal of tumors. Even though laparoscopy now has a limited function in tumor resection surgery, there are an increasing number of papers that support laparoscopic tumor resection [14-16]. The preliminary data do not point to a port-site recurrence of cancer, even if the investigations were not conducted over a long period of time or for a large number of patients [17].

Laparoscopy in Wilms' Tumor

Minimally invasive surgery (MIS) in the paediatric patients with cancers is gaining popularity. MIS is currently utilized for biopsies, assessment of tumor extent, second-look, as well as tumor exterpation. Though, only limited reports are available on experience with laparoscopy, increasing information is now available which favours successful laparoscopic tumor resection. Few long term reports on large group of patients are available but, at least, the preliminary reports are not indicative of higher risk of port-site recurrence of malignancy.

Due to a lack of accrual, a multi-institutional prospective randomised controlled study that intended to assess the function of MIS in children with paediatric malignancies was prematurely closed in 1998 [18].

A review of the causes that led to its termination revealed that nearly 40% of the surgeons weren't actively using MIS at their centres. Experts from all across the world drew attention to various controversies in the years that followed. These included inquiries into the appropriateness of lymph node sampling, the state of the surgical margins and GTR (gross total resection), the removal of big tumors, and other issues [19-21].

The SIOP Renal Tumor Study Group has also emphasised the inadequacy of lymph node sampling with the MIS technique [10]. The group has drawn comparisons between methods used with the MIS and open approaches. The excision of big tumors and sufficient lymph node sampling, however, continue to be the key issues [10]. There is insufficient evidence to justify MIS for paediatric renal tumors, according to a systematic review conducted by the American Paediatric Surgery Association (APSA) Cancer Committee [22]. Inadequate lymph node collection and a higher risk of intraoperative leak during MIS were the committee's top two concerns.

In an earlier report the author (MB) has addressed both these issue, i.e., successful excision of large tmours and adequacy of lymph node sampling by laparoscopy, utilizing appropriate techniques [23–24].

While there is currently no standard selection criteria for laparoscopic tumor excision in paediatric malignancies, the decision to use minimally invasive surgery should be made by a team of specialists including a paediatric surgeon, paediatric oncologist, and radiologist based on the individual patient's case and clinical characteristics. The surgeon's experience and knowledge are important factors in this decision-making process, but should not be the sole determining factors. The benefits and risks of laparoscopic surgery compared to open surgery should be carefully considered and discussed with the patient and family to make an informed decision.

It is important to note that while laparoscopy has shown promise in paediatric malignancies, its implementation should be carefully considered and performed by experienced surgeons. Further studies with longer follow-up periods and controlled trials are needed to evaluate the long-term outcomes and efficacy of laparoscopy in comparison to open surgery for solid malignancies. As the technology and techniques for laparoscopy continue to improve, its integration into future treatment protocols should be considered.

Conclusion

Lymph node sampling can also be performed effectively with laparoscopy. However, longer follow-up and multi-institutional controlled trials are needed to evaluate the long-term outcomes and to compare open versus laparoscopic surgery for solid tumors. Additionally, only surgeons with more experience in both paediatric oncology and laparoscopic surgery should perform the initial adoption of MIS in paediatric malignancies. The incorporation of laparoscopy in upcoming treatment protocols is encouraged given the advancements in laparoscopy and its careful application in paediatric cancers.

Conflicts of interest

The author declares that they do not have conflict of interest.

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ORIGINAL ARTICLE

HbA1c and Platelet indices correlation in type 2 diabetes patients

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Abstract

Background: Diabetes mellitus is a metabolic disorder represented by persistent hyperglycemia, which significantly elevates the risk of cardiovascular complications. Platelet dysfunction plays a crucial role in the development of these complications. While HbA1c is a widely employed diagnostic marker for diabetes, its association with platelet indices, reflecting platelet size and activity, in type 2 diabetes patients remains poorly understood. Recent research has increasingly emphasized platelet activation as a key contributing factor to atherothrombotic processes in individuals with diabetes.

Aim: Present study aims to find if there is any correlation between platelet indices and HbA1c.

Discussion: Hyperglycemia leads to reactive oxygen species and AGEs formation, resulting in endothelial dysfunction. The combination of increased intracellular calcium, decreased cAMP levels, and oxidative stress contributes to platelet hyperactivity. Endothelial dysfunction exacerbates this hyperactivity and manifests as an increase in platelet size and alterations in platelet indices.

Conclusion: Our research findings indicate that diabetes mellitus exhibits larger and more active platelets, resulting in an elevated thrombogenic potential. It also revealed a direct and positive correlation between platelet indices and HbA1c levels.

Keywords: HbA1c, MPV, PDW, P-LCR, Platelet indices

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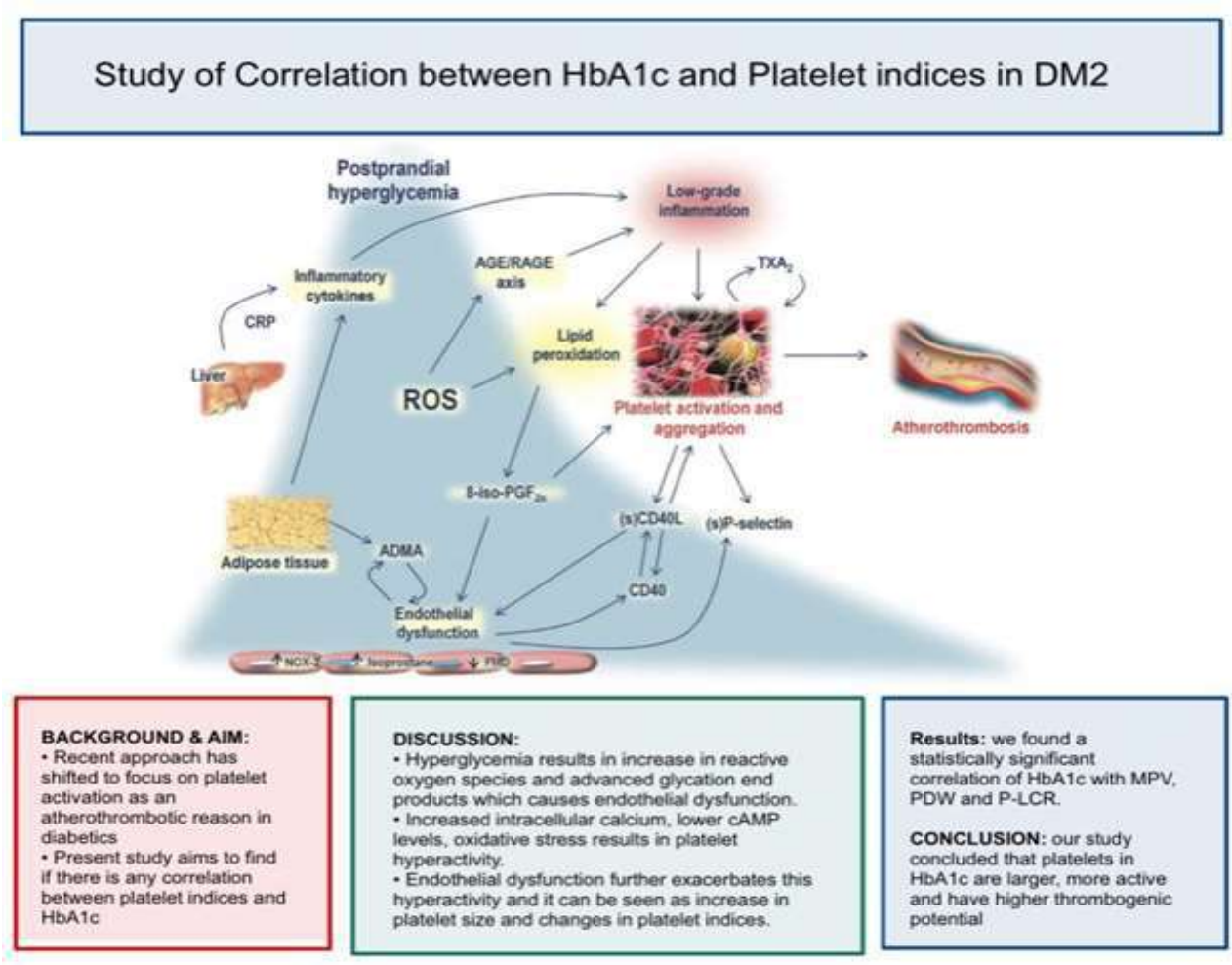
Abbreviations

AGEs	:	Advanced Glycation End products
P-LCR	:	Platelet-Large cell ratio
CBC	:	Complete Blood Count
cAMP	:	cyclic Adenosine Monophosphate
PDW	:	Platelet Distribution Width
HbA1C	:	Glycosylated Hemoglobin levels
MPV	:	Mean Platelet Volume

Graphical Abstract



Introduction

Diabetes is a long-lasting illness characterized by insufficient production or ineffective use of insulin by the body. As a consequence, uncontrolled diabetes can cause high blood sugar levels that gradually damage essential organs like the heart, blood vessels, eyes, kidneys, and nerves [1]. HbA1c serves as a useful indicator of average blood glucose levels over a three-month period [2]. Additionally, altered platelet shape, increased platelet dysfunction, and heightened

reactivity contribute to diabetes-related complications, creating a prothrombotic state that leads to vascular challenges, ultimately increasing morbidity and mortality [3]. Furthermore, diabetes triggers inflammation and accelerates the development of atherosclerosis, further contributing to its prothrombotic nature [4].

Pathophysiology of Diabetic Platelet

Diabetes mellitus is a prothrombotic condition indicated by impaired fibrinolytic capacity, coagulation system activation and persistent platelet activation. Hyperglycemia directly influences platelet reactivity through osmotic effects [5]. Protein kinase C which is a mediator of various platelet agonists involved in promoting platelet aggregation is activated by acute and chronic hyperglycemia. Advanced Glycation End products (AGEs) are created due to non-enzymatic contact between proteins and reducing sugars during recurrent periods of hyperglycemia. Some AGE molecules induce externalization of platelet membrane phosphatidylserines which in turn leads to surface clotting factors activation producing a thrombogenic state [6].

Hyperglycemia results in larger platelet size due to decreased cyclic adenosine monophosphate (cAMP) levels. In chronic diabetes patients, platelet intracellular calcium levels are elevated, leading to heightened platelet reactivity and aggregation even at lower levels of agonist activation. Interaction between lipids and glucose reduces nitric oxide synthesis because of formation of glycated low-density lipoprotein, which contributes to platelet hyperactivity [7].

Insulin directly regulates platelet function by interacting with the insulin receptor (IR) found on it. With insulin binding to IR, there is a trigger of tyrosine phosphorylation causing activation of insulin receptor substrate 1. This process elevates cAMP levels, thereby reducing P2Y12 signaling and platelet activity. Additionally, it also reduces platelet affinity to collagen hence decreasing the binding and platelet aggregation induced by agonists [8].

Platelets Indices:

Platelets count

The normal platelet count in a cubic centimeter of blood typically falls within the range of 150,000 to 400,000. Thrombocytosis indicates an elevated platelet count, while thrombocytopenia signifies a decrease in platelet count [9].

Mean Platelet Volume

Mean Platelet Volume (MPV) refers to the average size of platelets in the blood. It is determined by analyzing the distribution of platelet sizes in each sample. MPV is measured in femtoliters (fL) and is often included as part of a complete blood count (CBC) test. The normal range is 7 to 9 femtolitres.

MPV has gained clinical significance as a potential marker of platelet activation. MPV increase is associated with platelet hyperactivity, as larger platelets tend to be more reactive and have a higher thrombotic potential [10]. Platelet hyper-reactivity is manifested by enhanced aggregation, fibrinogen binding, and thromboxane production as shown in Figure 1. These variables change platelet metabolism and

interplatelet signalling, resulting in impairment of several metabolic processes, including ADP generation, thromboxane A2 synthesis/release and increased calcium metabolism.

Parameter	Description	Unit	Clinical utility
Mean Platelet Volume	Analyser calculated measure of thrombocyte volume	Femtoliters	Low MPV is associated with bleeding risk in TCP
Platelet Distribution Width	Indicator of volume variability in platelet size	Percentage (%)	No relation to bleeding risk in TCP
Platelet count	Indicates platelet number present in blood stream	Per cubic cm	Diagnostic for thrombocytopenia, risk of interference or lack of detection because of large clumps
Platelet - large cell ratio	Indicator of larger (>12 fL) circulating platelets	Percentage (%)	Dependant on platelet distribution curve

Figure 1. Various platelet indices and their clinical significance.

Elevated MPV has been observed in various conditions such as cardiovascular diseases, including myocardial infarction and stroke, as well as in inflammatory and autoimmune disorders. MPV can serve as an indicator of platelet turnover and activity, aiding in the diagnosis, prognosis, and monitoring of certain medical conditions. It may help identify individuals at higher risk for thrombotic events or predict the response to antiplatelet therapies [11].

Platelet Distribution Width

The variation in platelet size in a blood sample is measured by Platelet Distribution Width (PDW). It is typically reported as a percentage and is derived from analyzing the distribution of platelet volumes. PDW provides information about the heterogeneity of platelet sizes within the blood. Higher PDW values indicate increased variability in platelet sizes, suggesting a greater range of platelet activation and function [12]. The clinical significance of PDW lies in its potential as an indicator of platelet activation and associated disorders. Elevated PDW levels have been observed in conditions such as cardiovascular diseases, thrombotic events, and inflammatory disorders. It is believed that an increased PDW reflects presence of more reactive and larger platelets, which are associated with a higher thrombotic risk. PDW can serve as a complementary parameter to Mean Platelet Volume (MPV) in assessing platelet function and activity [13].

Platelet-Large cell Ratio

The proportion of large platelets in relation to the total platelet count in a blood

sample gives Platelet Large Cell Ratio (PLCR). It is calculated by dividing the number of large platelets by the total platelet count and multiplying by 100. PLCR is a parameter that provides information about the presence of larger platelets in the bloodstream. Large platelets, also known as macro platelets, are often indicative of increased platelet production and activity. They are released into the circulation in response to platelet turnover and various physiological or pathological conditions [14]. The clinical significance of PLCR lies in its potential as an indicator of platelet function and activation. Higher PLCR values may suggest increased platelet turnover and activation, which can be associated with conditions such as immune thrombocytopenia, myeloproliferative disorders, and inflammatory states. Additionally, PLCR has been studied as a prognostic marker in cardiovascular diseases, with elevated levels being associated with a higher risk of adverse outcomes [15].

HbA1c and Cardiovascular Complications

Diabetes significantly increases the risk of developing various cardiovascular complications, such as coronary artery disease, myocardial infarction, stroke, peripheral artery disease, heart failure and sudden cardiac death [16]. The underlying mechanisms linking diabetes to CVD are complex and multifactorial. Chronic hyperglycemia, insulin resistance, dyslipidemia, hypertension, endothelial dysfunction, and inflammation contribute to the development and progression of cardiovascular complications in individuals with diabetes [17]. They also have high levels of plasminogen activator inhibitors and fibrinogen, which promotes clotting and inhibits fibrinolysis, favoring thrombosis. HbA1c is widely used as a marker for glycemic control in individuals with diabetes [18]. Elevated HbA1c levels have been associated with an increased risk of CVD events, including myocardial infarction and stroke. Conversely, optimal glycemic control, reflected by lower HbA1c levels, has been associated with a reduced risk of CVD events and improved cardiovascular outcomes in individuals with diabetes.

Methods

For Platelet indices and HbA1c Estimation

A venous sample was collected using EDTA vials in the early morning to determine platelet indices and HbA1c levels. The estimation of platelet indices was performed using the ELITE-580, a fully automated hematology analyzer. Criteria for diagnosing Diabetes Mellitus is shown in Figure 2.

1. FBS ≥ 126 mg/dl with fasting (no calorie intake) for 8 hours
2. HbA1c ≥ 6.5%
3. 2 hr. post prandial blood glucose ≥ 200 mg/dl (OGTT 75g)
4. RBS ≥ 200 mg/dl with hyperglycemic crisis

Figure 2. Criteria for diagnosing Diabetes Mellitus [19]

HbA1c

HbA1c, also known as glycated hemoglobin, is formed when glucose reacts non-enzymatically with natural Hb (hemoglobin). The extent of this reaction is directly related to the concentration of glucose in the bloodstream. In hemolyzed blood, both total Hb and HbA1c bind to latex particles found in the R1 reagent. The degree of binding is proportional to the relative concentrations of these substances in the blood. The R2 reagent contains cross-linked antihuman HbA1c monoclonal antibodies that bind to the HbA1c bound to the particles. The resulting agglutination directly corresponds to the percentage of HbA1c present in the sample. A normal HbA1c value typically falls within the range of 4-6% [20].

Results

This study was conducted among 190 diabetic patients who came with either diabetes or related complications. The mean age of the study participants in our research was 56.3±11.04 years. Demographic distribution was maximum in age group of 41-60 years [105,55.3%] followed by age group of >60 years [68,35.8%]. Males were more affected [97,51.1%] than females [93,48.9%] with a ratio of 1.04:1. Ratio of cardiovascular complications was significantly high with as much as 41 patients out of 48 [85.4%] presenting with diabetic complications were of cardiovascular origin. The average duration of diabetes among the patients included in the study was 4.9 ± 4.4 years. Mean BMI was observed as 25.6 ± 4.2 kg/m^2 with most of them falling in obese category. We also observed elevated mean HbA1c (9.4 ±2.3), MPV (12.31 ±7.55), PDW (16.30±3.74) and P-LCR (40.96±10.11) values as shown in Figure 3.

Furthermore, our study revealed statistically significant positive correlations between HbA1c and MPV (r=0.698), PDW (r=0.606), and P-LCR (r=0.647). Conversely, a statistically significant negative correlation was observed between HbA1c and platelet count (r= -0.202) as shown in Figure 4.

HbA1c values of all patients were plotted against Platelet indices (Platelet count, MPV, PDW and P-LCR) individually in a scatter plot diagram for assessing the correlation with them which are shown in Figures 5, 6, 7 and 8.

Lab. Parameters	Mean	Median	SD	Minimum	Maximum	P-value
Hemoglobin (g/dl)	12.42	12.50	1.27	10.1	15.7	0.766
TLC (cells/µL)	8236.62	8360.0	1891.14	4200	11600	0.314
Platelets (lacs/µL)	2.28	1.97	0.77	1.39	5.42	.643
MPV (fL)	12.31	11.85	7.55	9.3	14.5	0.0001
PDW	16.3	15.9	3.74	9.9	26.5	0.0001
P-LCR	40.96	42.4	10.11	18.8	58.2	0.0001
HbA1c (%age)	9.46	9.0	2.34	6.5	15.0	0.0001
Triglyceride (mg/dl)	167.31	166.5	55.4	52.0	405.9	0.0001
Cholesterol (mg/dl)	163.17	157.5	51.76	52.0	293.0	0.0001
HDL (mg/dl)	39.51	39.0	10.99	13.0	102.0	0.0001
LDL (mg/dl)	90.16	88.5	42.66	11.8	197.8	0.0001
VLDL (mg/dl)	33.62	33.3	11.02	10.2	81.2	0.0001

Figure 3. Distribution of laboratory parameters among study participants.

Platelets indices	Pearson correlation coefficient	P-value
Platelets count	-0.202	0.005
MPV	0.697	0.0001
PDW	0.606	0.0001
P-LCR	0.647	0.0001

Figure 4. Correlation of HbA1c with platelets indices.

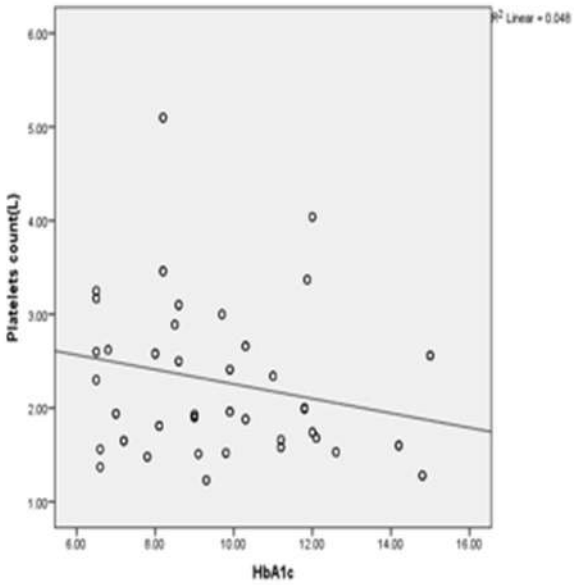


Figure 5. HbA1c vs Platelet Count.

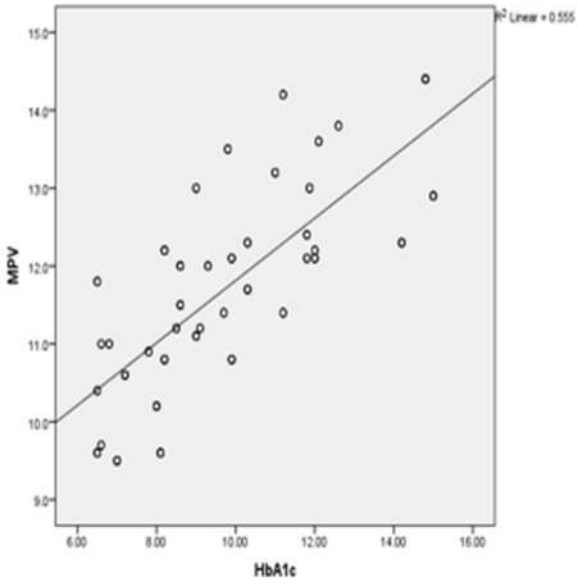


Figure 6. HbA1c vs MPV

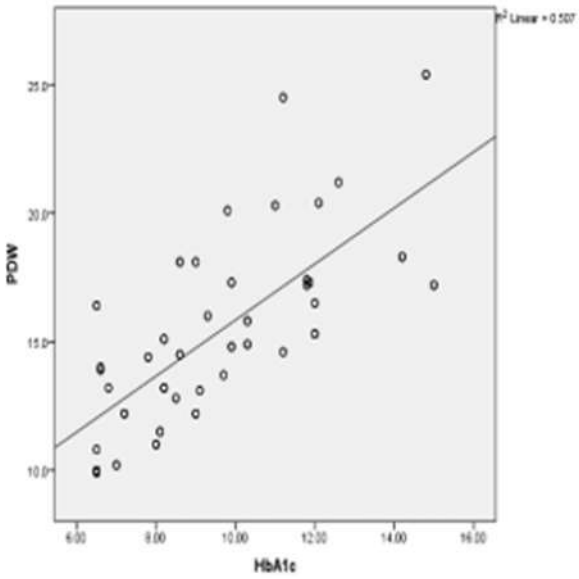


Figure 7. HbA1c vs PDW

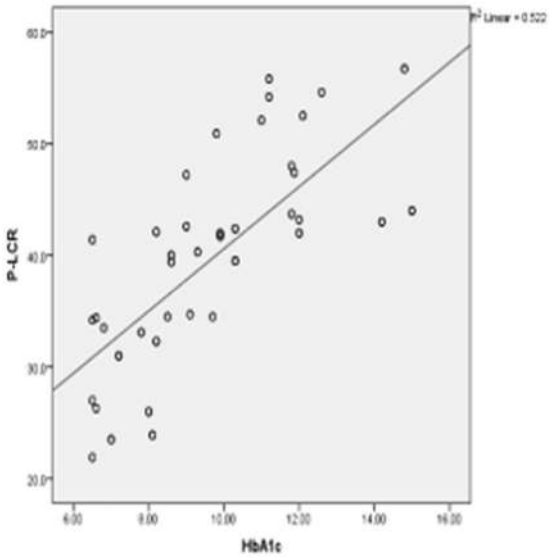


Figure 8. HbA1c vs P-LCR

Conclusion

Our research findings indicate that individuals with diabetes mellitus (DM) exhibit larger and more active platelets, resulting in an elevated thrombogenic potential and increased platelet indices. The presence of larger platelets constitutes a significant risk factor in the development of atherosclerosis and is closely linked to vascular complications. Additionally, a direct and positive correlation between platelet indices and HbA1c levels was found in this study.

Future scope

The future research potential of investigating the correlation between HbA1c and platelet indices in type 2 diabetes patients is highly promising. This exploration can provide valuable insights into the relationship between HbA1c, an essential long-term blood glucose control marker, and platelet indices, which indicate platelet size and activity. Understanding this connection has the potential to enhance our understanding of the pathophysiology and complications associated with diabetes. Furthermore, further research may lead to development of more accurate diagnostic and prognostic tools for assessing cardiovascular risk and guiding therapeutic interventions for type 2 diabetes patients. Moreover, by unraveling the mechanisms underlying the association between HbA1c and platelet indices, new therapeutic strategies could be devised to modulate platelet function and reduce the risk of vascular complications. Continued research efforts in this field have the capacity to advance our knowledge of diabetes-related thrombogenesis leading to improved patient outcomes.

Conflicts of interest

The authors declares that they do not have conflict of interest.

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ORIGINAL ARTICLE

Histomorphological Analysis of Testicular Specimens at Tertiary Care Hospital in Western Rajasthan – A Retrospective Study

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Abstract

Introduction: Numerous etiologies, categorised as Neoplastic and Non-Neoplastic lesions, can affect the testis. Non-neoplastic conditions are further broken down into important categories such as congenital anomaly, inflammation or infection, vascular disorders, and atrophy caused by various etiologies. Neoplastic lesions are far less common than non-neoplastic lesions, but their early detection is crucial for managing them and understanding age distribution.

Objectives: Our study aims to analyze Histomorphological spectrum of various testicular specimens as well as to calculate age incidence of various testicular lesions.

Material and Methods: This retrospective study of five years from January 2017 to December 2021 with total of 100 specimens conducted in department of pathology of jhalawar medical college. All orchidectomy specimens managed further and examined microscopically.

Results: Overall, it was discovered that non-neoplastic lesions were more prevalent than neoplastic lesions (85% vs. 15%). The most frequent non-neoplastic lesions were torsion/infarction (38%), followed by both cryptorchidism (14%) and Non specific inflammatory lesions (14%). Seminoma (40%) is more frequent than embryonal carcinoma (26.67%) among neoplastic tumours, which is thought to be the second most frequent. Inflammatory lesions are substantially less common among younger age groups, according to our research.

Conclusion: Comparing histopathogical evaluation to recently developed molecular techniques, we found it to be a very simple, logical, and effective instrument. It turns out to be quite useful for both identifying different testicular lesions and categorising their age occurrences.

Key words*:* Orchidectomy, Testicular Lesions, Torsion, Seminoma

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Introduction

A wide variety of non-neoplastic and neoplastic lesions can affect the testicles. Neoplastic lesions are less common to arise than non-neoplastic lesions, nonetheless. using tumour markers assays or ultrasonography as support for various non-invasive treatments while using histomorphological inspection as a key first resource in improving treatment decision-making. The epidemiology of distinct testicular non-neoplastic and neoplastic lesions varies greatly across different geographic borders. Worldwide, it is estimated that 1-2% of children aged 3 to 12 months have undescended testes or have cryptorchidism. In a similar vein, neoplastic lesions like germ cell tumours, which most frequently affect people between the ages of 15 and 45, account for only 1-2% of all male malignant tumours [1, 2, 3].

Congenital abnormalities, infertility, inflammation and infection (Epididymitis, Orchitis of various origin), vascular disorders (systemic vasculitis, varicocele, torsion and infarction), atrophy, and other non-neoplastic pathologic conditions all affect the testis [4].

The testis is affected by a variety of cancers, but their occurrence is considerably lower than that of benign or non-cancerous illnesses. These cancers can be further divided into germ cell tumours of the testis (Seminoma, Yolk sac tumour, Teratoma, etc.), non-germ cell tumours, and secondaries [15].

Material and Methods

100 testicular specimens in total were received at the pathology department of the Jhalawar Medical College and Hospital throughout a five-year period from January 2017 to December 2021. Samples were fixed in 10% formalin. Following a gross evaluation, the tissue was treated using an automated tissue processor, which included paraffin embedding, sectioning, and hematoxylin and eosin staining. According to WHO categorization, various lesions will be histomorphologically categorised.

Inclusion Criteria

Simple orchidectomy specimens, Bilateral simple orchidectomy specimens, Radical orchidectomy specimens and high inguinal orchidectomy specimens received in Pathology Department, Jhalawar medical college and Hospital, Jhalawar.

Exclusion Criteria

Biopsies received for infertility evaluation are excluded from study.

Methodology

Only those patients who meet the inclusion and exclusion criteria will be enrolled for the study after receiving approval and clearance from the ethical committee.

Gross Examination

1. When orienting the specimen, keep in mind that the epididymis can be felt superiorly and posteriorly, and that the cord structures pass superiorly.
2. Measure both the specimen and the length of the cord.

3. Beginning at the spermatic cord's tip, ink the cord cut margin.
4. Separate the testis into many parallel pieces starting from the base of the cord and moving toward the tunica. sufficient fixing portions. Fix the sample for 12 to 24 hours.
5. After fixing, cut a whole portion of the specimen's cord-cut margin after determining its separation from the tumor's or the cord's base.
6. Examine and characterise the tumor's size, shape, colour, texture, and areas of necrosis and haemorrhage. Keep an eye out for the development of hair, cartilage, bones, and teeth.
7. Visually evaluate the tumor's size in respect to the tunica layers, the epididymis, the rete testis, and the cord's base.
8. Before submitting sections from the tumour, take sections from the cord's base.
9. Take sections of the tumour for microscopic examination: one section for every cm of the tumour; sections with layers of tunica; sections with rete or epididymis; portions with any remaining native testicular tissue.
10. If the surgeon has sent a primary retroperitoneal lymph nodal dissection, gross the nodes and submit them.

Observation and Results

In the present study most common lesion was found to be torsion and infarction accounting for 38 cases, 38% (n = 100) followed by next common both cryptorchid lesion and Non specific inflammatory lesions recorded for 14 cases each, 14%. The other lesions with their incidence are classified in Table 1.

Table 1. Histomorphological Lesions Among Testicular Specimens.

HISTOMORPHOLOGICAL DIAGNOSIS	CASES
NEOPLASTIC	
SEMINOMA	6
EMBRYONAL CARCINOMA	4
TERATOMA	3
YOLK SAC TUMOR	2
NON NEOPLASTIC LESIONS	
NORMAL	8
CRYPTORCHID	14
TORSION AND INFARCTION	38
ATROPHY	4
NON SPECIFIC INFLAMMATORY LESIONS	14
TUBERCULAR ORCHITIS	1
ABSCESS	6
TOTAL	100

In this study it is observed that out of 100 cases, 85 cases reported for non neoplastic lesions (85%) and 15 cases were reported for neoplastic origin (15%). Among all age groups incidence of non neoplastic lesions are higher compared to neoplastic lesions, incidence of neoplastic lesion among age group >60 years is nil as not a single neoplastic lesion reported under this group (Table 2).

Table 2. Incidence of Neoplastic and Non neoplastic Lesions age group wise.

LESIONS	0-20 Years	21-40 Years	40-60 Years	>60 Years	Overall Percentage
	(n = 27)	(n = 35)	(n = 26)	(n = 12)	(n = 100)
NON NEOPLASTIC LESIONS	92.59%	74.29%	84.62%	100%	85%
NEOPLASTIC LESIONS	7.41%	25.71%	15.38%	0	15%

Among age group 0-20 years there is equal incidence of embryonal carcinoma and yolk sac tumor as 6.67%, in group 21-40 years incidence of seminoma is higher as 26.67%, not a single neoplastic case is reported in group >60 years. Among neoplastic lesions seminoma is the most common lesion in present study (Table 3).

Table 3. Incidence of Different neoplastic lesions age group wise.

NEOPLASTIC LESIONS	0-20 Years	21-40 Years	40-60 Years	>60 Years	Overall Percentage
(n = 15)					
SEMINOMA	0	26.67%	13.33%	0	40%
EMBRYONAL CARCINOMA	6.67%	13.33%	6.67%	0	26.67%
TERATOMA	0	13.33%	6.67%	0	20%
YOLK SAC TUMOUR	6.67%	6.67%	0	0	13.33%
OVERALL PERCENTAGE	13.33%	60.00%	26.67%	0	

Table 4. Incidence of Different Non neoplastic lesions age group wise.

NON NEOPLASTIC LESIONS	0-20 Years	21-40 Years	40-60 Years	>60 Years	Overall Percentage
	(n = 85)				
NORMAL	0	1.18%	3.53%	4.71%	9.41%
CRYPTORCHID	1.18%	7.06%	4.71%	3.53%	16.47%
TORSION AND INFARCTION	28.24%	11.76%	4.71%	0	44.70%
ATROPHY	0	2.35%	0	2.35%	4.71%
NON SPECIFIC INFLAMMATORY LESIONS	0	5.88%	9.41%	1.18%	16.47%
TUBERCULAR ORCHITIS	0	1.18%	0	0	1.18%
ABSCESS	0	1.18%	3.53%	2.35%	7.06%
OVERALL PERCENTAGE	29.42%	30.59%	25.88%	14.12%	

In age group 0-20 years most common non neoplastic lesion found to be torsion or infarction with incidence of 28.24%, In 21-40 years of age group most common lesion is again torsion or infarction with 11.76%, in group 40-60 years Non Specific inflammatory lesions (9.41%) are most common, In group >60 years most testis are having normal architecture done mainly for hormonal ablation in prostatic carcinoma (Table 4).

Discussion

In present study most common lesion among non neoplastic group is found to be torsion or infarction including gangrenous testis with incidence of 44.70% followed by both cryptorchidism and inflammatory etiology with an incidence rate of 16.47% respectively in total of 85 non neoplastic lesions which is comparable Baidya R et al. [20] with incidence of Torsion or infarction as 54.90%, There is quite variation in incidence of different non neoplastic lesions because of various geographical and environmental factors or boundations. (Table 5).

Among neoplastic lesions most common lesion is found to be seminoma with an incidence rate of 40% followed by embryonal carcinoma having incidence rate of 26.67% among total of 15 cases of neoplastic origin in comparison to other studies Buge Aarti el al [10] Seminoma is common with incidence of 37.5%, Tekumalla A et al [13] again seminoma is most common with incidence of 40%, In Baidya R el al [20] seminoma is the most common lesion (44.44%) Among neoplastic lesions seminoma is the most common lesion in almost all the studies which is comparable to our study (Table 5).

Table 5. Comparison of different Histomorphological lesions in different studies.

NON NEOPLASTIC LESIONS	Buge Aarti et al (2020) Maharashtra	Tekumalla A et al (2019) Telangana	Baidya R et al (2017) North East	Mansi Sharma et al (2017) Jammu	Present Study
	(n = 31)	(n = 65)	(n = 51)	(n = 53)	(n = 85)
NORMAL	0.00%	21.50%	0.00%	0.00%	9.41%
ABSCESS	12.90%	0.00%	15.68%	5.66%	7.06%
ATROPHY	12.90%	23.10%	0.00%	16.98%	4.71%
CRYPTORCHID	9.68%	4.60%	7.84%	39.62%	16.47%
INFLAMMATORY ETIOLOGY	32.26%	38.50%	9.80%	15.09%	16.47%
TUBERCULAR ORCHITIS	9.68%	0.00%	9.80%	3.77%	1.18%
TORSION/INFARCTION/GANGRENOUS	16.13%	12.30%	54.90%	18.86%	44.70%
OTHERS NON NEOPLASTIC	6.45%	0.00%	1.96%	0.00%	0.00%
NEOPLASTIC LESIONS	(n = 8)	(n = 15)	(n = 9)	(n = 4)	(n = 15)
TERATOMA	25.00%	13.34%	11.11%	25.00%	20.00%
SEMINOMA	37.50%	40.00%	44.44%	25.00%	40.00%
EMBRYONAL CARCINOMA	0.00%	0.00%	0.00%	0.00%	26.67%
YOLK SAC TUMOUR	0.00%	6.67%	0.00%	25.00%	13.33%
OTHERS NEOPLASTIC	37.50%	40.00%	44.44%	25.00%	0.00%

In present study it is observed that out of 100 cases, 85 cases reported for non neoplastic lesions (85%) and 15 cases were reported for neoplastic origin (15%) which is comparable with other studies stated in Table 6.

Table 6. Comparison of Non Neoplastic and Neoplastic lesions in different studies.

STUDIES	Non Neoplastic Lesions	Neoplastic Lesions
Tekumalla A et al (2019)	81.25%	18.75%
Ali Abdul Latheef et al (2019)	91.30%	8.70%
Kalpana R et al (2018)	92.86%	7.14%
Charak A et al (2018)	90.20%	9.80%
Baidya R et al (2017)	85.00%	15.00%
Hemavthi Reddy et al (2016)	86.00%	14.00%
Present Study	85.00%	15.00%

Conclusion

There is a wide diversity of histopathology in testicular lesions. Compared to neoplastic lesions, Non neoplastic lesions are substantially more prevalent. The most frequently researched non-neoplastic lesion is torsion or infarction. Seminoma is the most prevalent neoplastic lesion. All age groups experience non-neoplastic lesions on a regular basis, however as people age, the frequency of neoplastic lesions declines. As clinical or USG findings may mistake a neoplastic lesion for a non-neoplastic one or vice versa, histopathological diagnosis is thought to be the gold standard method for making a final determination regarding the diagnosis of various testicular lesions. Most of the differences between our study and other studies are attributable to the differences in sample sizes, as well as geographic and environmental boundaries.

Statements and Declarations

Competing Interests – No Direct or Indirect financial aid was taken to conduct this study.

Conflict of Interest – No conflict of interest.

Author Contributions

Dr. Viral Jain – Study Conception and Design Along With Data Collection

Dr. Richa Sharma – Reporting of Cases with Analysis of Results

Dr. Rishi Diwan - Reporting of Cases with Draft Preparation

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ORIGINAL ARTICLE

NLR, CRP, LDH as severity markers in Coronavirus Positive patients

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Abstract:
Background: Coronavirus is a deadly respiratory virus and was discovered way back in 1965 but made a recent comeback in November- December 2019. In March 2020, coronavirus infection was declared a pandemic, since then there has been widespread research taking place on this virus. For confirmatory diagnosis of coronavirus infection, Rapid Antigen detection test, TRUNAAT, RTPCR are used.
Aim: Correlation of NLR, CRP, LDH as a marker of severity, morbidity, and mortality of coronavirus positive patients.
Discussion: Coronavirus has undergone multiple small changes in its RNA genome known as mutation leading to production of variants. A lot of variants have been produced and detected since then because of its high replicability and mutation rate. The more dangerous variants have been labelled as Variants of Concern and less severe variants have also been detected which are known as Variants of Interest. Although, a viral infection is usually associated with lymphocytosis in most cases, but coronavirus infection has been reported to be associated with lymphopenia.
Conclusion: There is a significant correlation of Neutrophil to Lymphocyte Ratio, S.CRP, S.LDH with the severity of coronavirus disease. They can be used individually as well as in combination as markers to establish severity of the coronavirus disease and helps in deciding prognosis of the patient.

Keywords- NLR, coronavirus, severity marker, CRP, LDH

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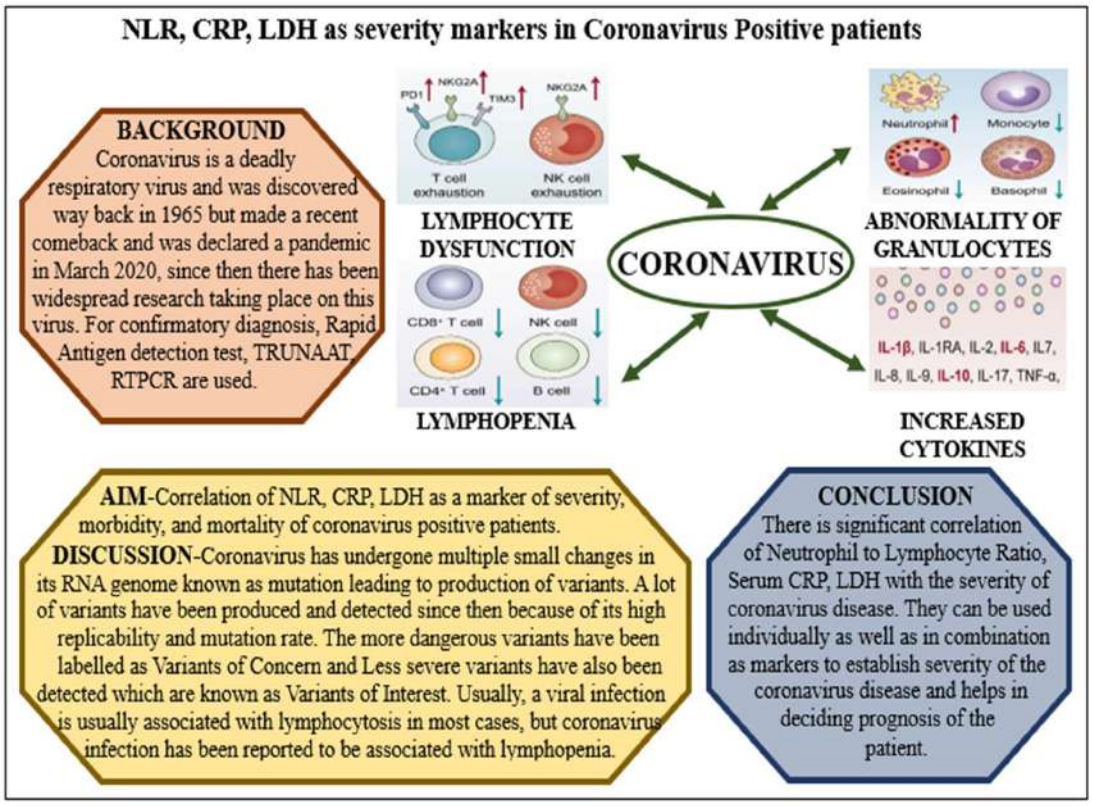
Abbreviations

LDH	:	Lactate Dehydrogenase
CRP	:	C-Reactive Protein
NLR	:	Neutrophil to Lymphocyte Ratio
RNA	:	RiboNucleic Acid
TRUNAAT	:	Taqman Cartridge Based Nucleic Acid Amplification Test
CoV	:	Coronavirus
SARS	:	Severe Acute Respiratory Syndrome
RTPCR	:	Reverse Transcriptase Polymerase Chain Reaction
ACE	:	Angiotensin Converting Enzyme
HRCT	:	High Resolution Computed Tomography
CTSS	:	Computed Tomography Severity Score

Graphical Abstract



Introduction

Coronavirus is a deadly respiratory virus and was discovered way back in 1965 but made a recent comeback in November-December 2019 which belonged to same lineage (A lineage is a group of closely related viruses with a common ancestor) [1]. In March 2020, coronavirus infection was declared a pandemic, since then there has been widespread research taking place on this virus. Coronavirus has undergone multiple small changes in its RNA genome known as mutation leading to production of variants. A lot of variants have been produced and detected since then because of its high replicability and mutation rate.

For confirmatory diagnosis of coronavirus infection, few antigens and nucleic acid-based tests are advised that are Rapid Antigen detection test, TRUNAAT,

RTPCR. Out of these, TRUNAAT and RTPCR work based on detection of nucleic acid of the virus by amplifying it several times via PCR [2].

Pathophysiology

Sars-Cov2 is transmitted via aerosol droplets from an infected individual. Once transmitted, it goes to upper respiratory tract and get bound to ciliated epithelial cells with the help of spike protein 1. Spike protein 2 helps in fusion with host cell membrane. After fusion, it transmits nuclear material (+ssRNA) to host cell which in turn produce a negative strand of ssRNA and then undergoes viral replication. After newer RNA copies are made from negative strand via RNA polymerase activity, it also produces nucleocapsid and other viral packaging proteins [3]. New viral particles are released via exocytosis ready to infect new respiratory host cells and cause induction of apoptosis in the lymphocytes by indirect mechanisms such as soluble Fas ligand (sFasL), vascular cell adhesion molecule-1 (VCAM-1) [4].

In almost 80% of cases, the infection is contained in upper respiratory tract but in rest 20% cases it may invade lower respiratory tract. It has a special affinity towards ACE-2 receptors which are found on type 2 pulmonary alveolar epithelial cells. After the invasion, it leads the host cells to produce a series of inflammatory cytokines like IL-6, TNF-α etc. The cytokines are associated with increased production of neutrophils in the bone marrow and cause recruitment of CD4 and CD8 cells resulting in systemic inflammation [5]. Although, a viral infection is usually associated with lymphocytosis but coronavirus infection has been reported to be associated with lymphopenia [6]. CD8 mediated cytotoxicity and sequestration of inflammatory cells in the lungs leads to diffuse alveolar damage which finally causes the dreaded Acute Respiratory Distress Syndrome as shown in Figure 1 [7].

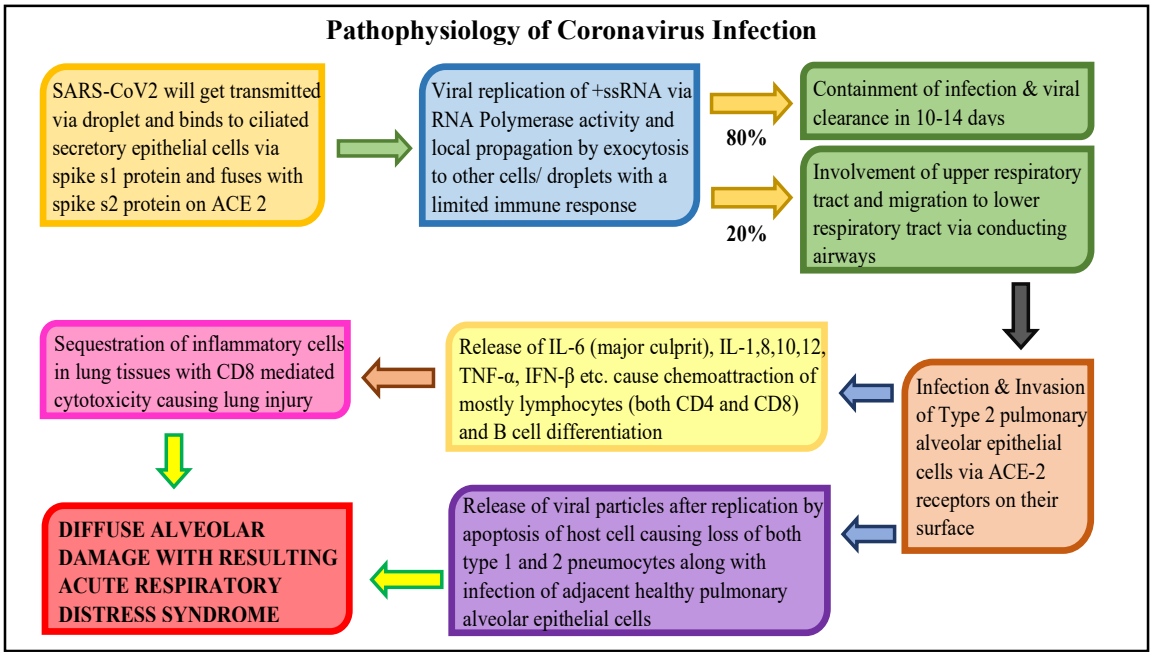


Figure 1. Pathophysiology of coronavirus infection and mechanism of ARDS

Variants of Concern

The more dangerous CoV2 variants are categorised as Variants of Concern as shown in Figure 2. It is based on ability to cause more severe disease like increased hospitalizations or deaths, evidence of increase in transmissibility, reduced effectiveness of treatments or vaccines, significant reduction in antibody mediated neutralization generated during previous infection, or diagnostic detection failures [8].

Variants of Interest

Less severe variants are categorised as Variants of Interest as shown in Figure 3. These are labelled based on reduced efficacy of treatments, reduced neutralization by antibodies generated against previous infection/vaccination, evidence of mutations causing altered receptor binding, predicted increase in transmissibility or potential diagnostic impact [9].

Figure 2. Variants of Concern

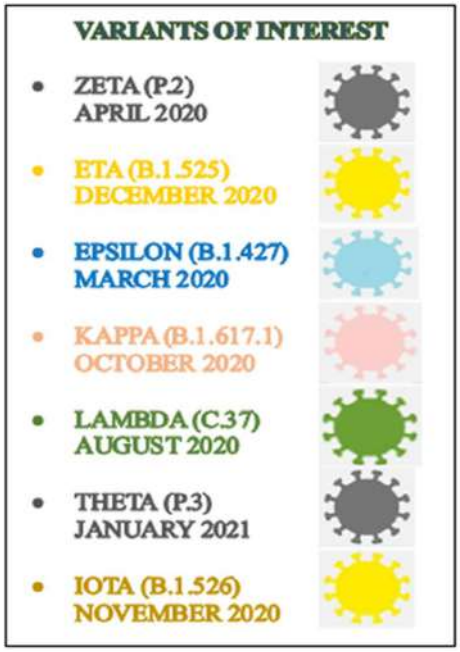


Figure 3. Variants of Interest

Clinical Features

Mild coronavirus illness

1. Mild symptoms such as fever, sore throat, nasal discharge, headache, malaise, cough, muscular pain, nausea, loose stools, loss of olfactory/gustatory sense.
2. SpO_2 >94% on room air,
3. Respiratory rate < 24 per minute,
4. No abnormal radiological imaging.
5. Also, no evidence of end organ damage or other severe comorbidities [10].

Moderate coronavirus illness

1. Shortness of breath,
2. SpO_2 = 90-94% on room air,
3. Respiratory rate between 24-30/min,
4. PaO_2/FiO_2 > 300 mmHg.
5. Infiltrates < 50% in HRCT (CTSS ≤12/25)[10]

Severe coronavirus illness

1. Shortness of breath,

2. SpO_2 < 89% on room air,
3. Respiratory rate > 30 times/min,
4. PaO_2/FiO_2 < 300mm Hg
5. Infiltrates > 50% in HRCT (CTSS ≥13/25) [11]

Critical Illness

The last but the most lethal presentation of coronavirus infection is critical illness which is defined as when the patients is suffering from (ARDS) acute respiratory distress syndrome, cardiac dysfunction, septic shock, elevation of inflammatory cytokine levels thus provoking a cytokine storm, and/or exacerbation of underlying co-morbidities that are already existing in the patient [12].

CT Severity Score

CTSS also known as CT Severity Score is a scale to quantify the lung involvement in coronavirus positive patients. Both lungs contain 5 lobes in total (3 in right lung and 2 in left lung) which are scored according to extent of involvement in each lobe between 0 to 5. The total score of all 5 lobes is the resultant score with a minimum score of 0 denoting no lung involvement and 25 denoting complete lung involvement. It has been widely used for quantifying the severity of covid illness and in predicting the prognosis also [13].

Markers of severity for Coronavirus disease

Neutrophil to Lymphocyte Ratio (NLR)

Neutrophil-to-lymphocyte ratio (NLR) is calculated by dividing the absolute/ percentage neutrophil count with absolute/ percentage lymphocyte count. Based on general trend in normal population, neutrophils are usually more in number than lymphocytes, so the normal ratio comes out to be greater than one [14].

Lactate Dehydrogenase (LDH)

LDH is a universal intracellular enzyme which is found as 5 different isozymes:
Type 1 in cardiac muscle cells,
Type 2 in reticuloendothelial cells and is also highest isoenzyme component,
Type 3 rich in lung tissue,
Type 4 found in kidneys & pancreas and
Type 5 in hepatocytes and striated muscle cells [15].

Since LDH's type 3 isoenzyme is present in pneumocytes, patients with coronavirus infection usually involving lungs produces large amount of LDH and increase the serum LDH levels, although whether it is only type 3 component is not determined. Additionally, LDH levels are elevated in thrombotic microangiopathy which is also seen in coronavirus infection, so other isoenzyme components of LDH can also be contributing factors in total serum LDH levels [16].

Normal Reference Range:
Serum LDH: < 248 IU/L.

C-Reactive protein (CRP)

CRP is a proteinaceous compound and is also an acute phase reactant produced in liver in response to inflammation. It has a regulatory mechanism controlled by cytokines IL1 and IL6 at transcriptional level. In recent studies, it is seen that the acute respiratory distress syndrome in Coronavirus infected patients is due to hyper-inflammation supported by cytokine storm which specially includes IL-6 and IL-1, hence making CRP a reliable marker for assessment of severity of coronavirus infection [17].
Normal Reference Range:
Serum CRP: 0-5 mg/L.

Methods

For NLR Calculation

Method: 2 ml fresh EDTA sample was taken using all aseptic precautions and was processed in fully automated 5-part Haematology Analyzer:

Result: The reports of samples from the analyser were used to calculate NLR by dividing absolute/percentage value of neutrophils and lymphocytes. The same were confirmed by peripheral blood film checked by the Pathologist under the microscope.

For CRP and LDH calculation

Sample: 2 ml fresh sample was collected using all aseptic precautions and serum was then separated by centrifuging the sample at 2500-3000 rpm. Sample was processed on fully Automated Biochemistry Analyzer.

Method for CRP: We had taken Immuno-turbidimetric test for quantitative determination of serum CRP levels. When serum was mixed with R1 buffer and R2 latex suspension, CRP reacts specifically with anti-human CRP antibodies coated with latex particles to yield insoluble aggregates. The absorbance of the aggregates was proportional to CRP concentration in serum.[18]

Method for LDH: LDH catalyses the oxidation of lactate to pyruvate coupled with reduction of NAD+ to NADH. The increase of NADH was measured at 340 nm which was directly proportional to enzyme activity in serum.[19]

Results

The study was conducted amongst 90 patients enrolled in the study who presented to GMSH, Sector 16, and Chandigarh as in patients or in OPD of medicine department. Out of 90 patients, 47 patients were found to be RTPCR positive whereas 43 patients were tested RAT positive. All the patients included in this study were adults and of age more than 18 years. The mean age of the study group was found to be 45.02 years. While comparing the male to female number in all 90 coronavirus positive patients, 51 (56.6%) patients were male and 39 (43.4%) were females with the ratio coming to 1.3:1. Analysis of data found that 49 (54%) patients belonged to mild category, 23 (26%) belonged to moderate category and 18 (20%) belonged to severe category.

Severity of the disease vs NLR

NLR was found to be positively correlated with severity index of the disease. Mean ± SD of NLR in mild, moderate, and severe cases were 2.62 ± 1.68, 4.86 ± 3.25 and 9.32 ± 5.48 respectively. NLR was significantly high in severe cases as compared to mild/moderate cases (p-value <0.005). Similarly, NLR was significantly high in moderate cases as compared to mild cases (p-value = 0.004).

Severity of the disease vs S.CRP

CRP and severity of the disease was positively correlated. Mean ± SD of CRP in mild, moderate, and severe cases were 4.6 ± 4.4, 56.9 ± 30.5 and 180.4 ± 61.5 respectively. CRP was significantly high in severe cases as compared to mild/moderate cases (p-value <0.005). Similarly, CRP was significantly high in moderate cases as compared to mild cases (p-value <0.005).

Severity of the disease vs S.LDH

LDH and severity of the disease was positively correlated. Mean ± SD of LDH

in mild, moderate, and severe cases were 217.2 ± 26, 289.2 ± 76.8 and 481.1 ± 165 respectively. LDH was very significantly high in severe cases as compared to mild/moderate cases (*p*-value <0.005). Mild cases had their LDH value within normal range.

Conclusion

In our study, there was significant degree of correlation of NLR, S.CRP, S.LDH with the severity of coronavirus disease. They can be individually used as markers to establish the severity and helps in deciding prognosis of the patient.

Future Scope

There is still ongoing emergence of new variants of coronavirus like Arcturus variant (formerly XBB 1.16) which are difficult to detect because of similarity with influenza virus. Hence, more effective clinical criteria's and diagnostic tools are required for early and specific detection. Vaccine development is an important area to work upon for eradication of coronavirus pandemic. Various DNA, RNA vaccines are under the research and will benefit the humanity once approved. Therapeutic drugs which are effective in severe covid are yet to be approved and are in different research phases. Long term covid and post covid adverse effects are yet to be fully understood and needs a lot of research tools.

Overall, the world has come a long way since the start of pandemic but there many more challenges in the way to come.

Conflicts of interest

The authors declares that they do not have conflict of interest.

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REVIEW ARTICLE

A Narrative Review on Forensic Toxicology of Human Hair and Nails

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Abstract
Forensic trichology is the study of hair evidence in criminal investigations, helping identify individuals and provide insights into their activities and associations. Forensic onychology, or forensic nail examination, involves analyzing nail evidence to determine factors like cause of death, drug use, or occupational history, assisting in uncovering critical information in forensic investigations. The analytical toxicology of human hair and nails has advanced significantly in recent years, allowing for a more accurate and comprehensive assessment of exposure to drugs, chemicals, and other toxic substances. Hair and nails are increasingly employed as matrices for the detection of new pharmacological targets because of their special qualities, such as their capacity to absorb and store xenobiotics for extended periods of time. However, interpreting the evidence in this area is overly complex and requires strong forensic expertise and adherence to strict scientific protocols. This review will discuss current research in forensic tricho-toxicology and forensic onycho-toxicology.

Keywords: Crime, Forensic Toxicology, Nails, Xenobiotics, Hair Preparations, Poisons

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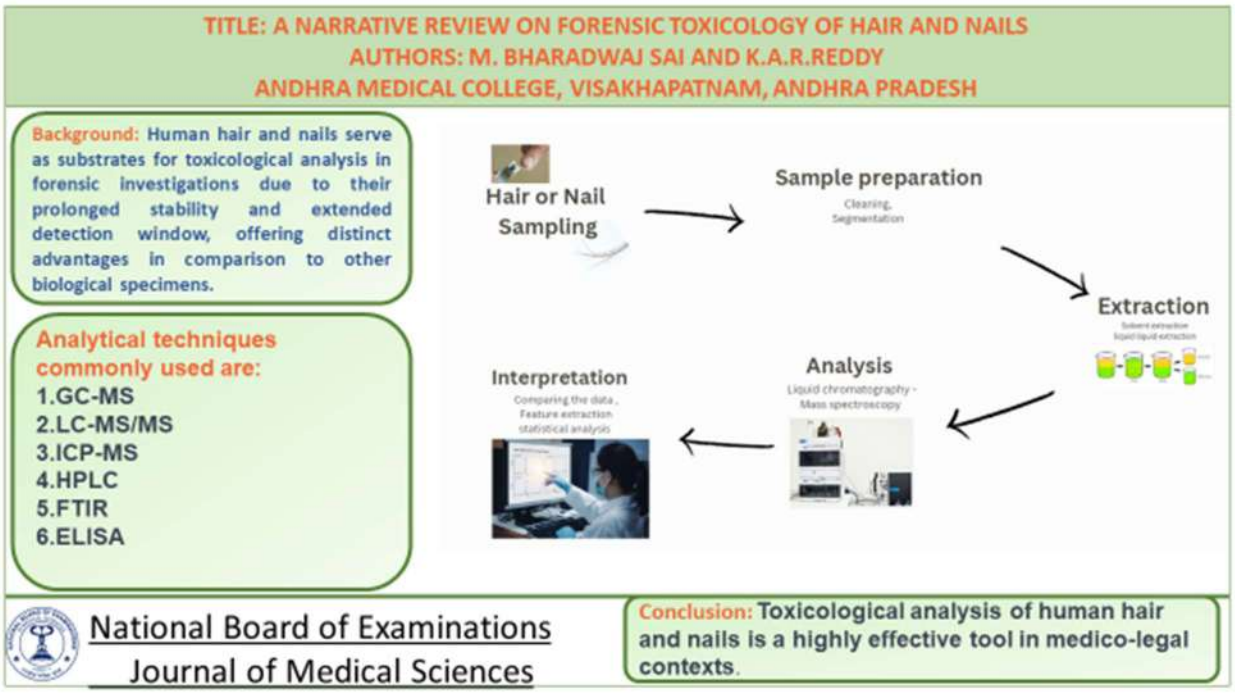
Graphical Abstract



Background

In forensic toxicology, human hair and nails are increasingly being employed as matrices for detecting drugs and toxicants because of their ability to incorporate drugs of abuse for a long duration of time. The history of a person's drug usage or exposure can be inferred retroactively from the hair and nails, which are non-invasive matrices for analysis. In this brief review, we present the most recent studies in the fields of forensic tricho-toxicology and onycho-toxicology along with some future perspectives of research. It is quite uncommon for forensic practitioners to consider hair and nails for toxicological investigations both in the living and the dead. There is a strong need for the dissemination of information on this subject amongst medical legal practitioners [1–3].

Discussion

Hair is a filamentous structure that grows from follicles in the skin. It consists of three layers: the cuticle, cortex, and medulla. The hair follicle beneath the skin contains the papilla, bulb, and root. Nails are composed of the nail plate, nail bed, lunula, and cuticle. The nail plate is the visible part made of tightly packed cells. The nail bed is the skin beneath the nail plate, while the lunula is the crescent-shaped area at the base. The cuticle protects the nail base, and the nail bed supports nail growth. The proximal hair shaft and the nail plate are ideal samples for toxicological analysis (Figure 1).

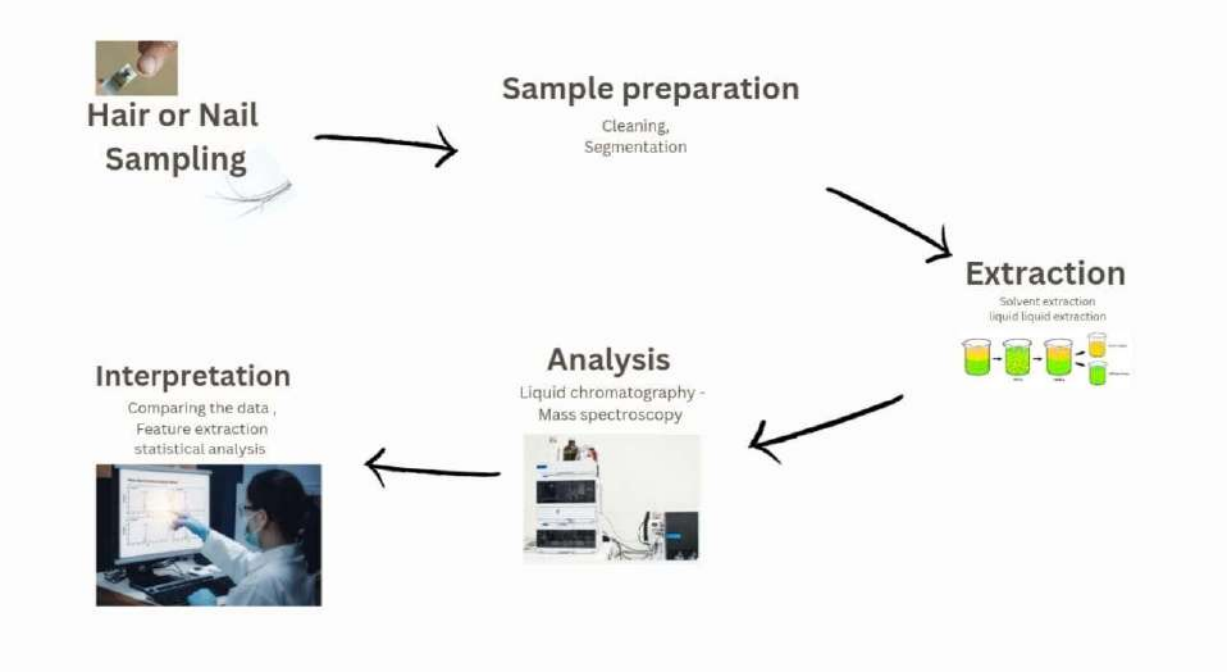


Figure 1. Basic workflow of Toxicological analysis of hair and nails

The collection and processing of hair and nails plays a crucial role in ensuring the accuracy and reliability of analytical toxicology findings. To achieve optimal results in analysis, it is recommended to collect dry samples of hair with roots intact and whole nails. These specimens do not require specific preservatives, although precautions should be taken to prevent fungal contamination. In recent times, advancements in hair and nail sampling and preparation techniques have enabled the examination of lower sample volumes with improved sensitivity and specificity. This progress has been instrumental in enhancing our ability to spatially study drug distribution in hair and nails. Methods such as imaging mass spectrometry and micro-segmental hair analysis have emerged, allowing for the investigation of drug distribution patterns within these matrices. These advancements have contributed to greater precision and a deeper understanding of drug incorporation and deposition in hair and nails [4-7].

One in every five deaths worldwide (11.8 million per year), is reportedly caused directly or indirectly by substance use, according to a statistical report covering the years 1990 to 2019. 1.65 million people lost their lives in India every year due to the drug menace. According to data provided by the World Health Organization, around 270 million people, or 5.5% of the world's population, between the ages of 15 and 64, took psychoactive drugs in the preceding year, and thirty-five million people are thought to be affected by drug use disorders. Drug use or consumption accounts for 75% of all occurrences of predatory rape, which causes unconsciousness and impairs the victim's capacity to consent to sex [8,9].

In forensic toxicology, human hair and nails serve as a good sample to represent chronic exposure to different substances. The history of a person’s drug abuse or exposure can be inferred retrospectively from the hair and nails, which are considered the best non-invasive matrices. Numerous research articles have explored the long inspection

window of hair and nails as a means to examine drugs and toxins. In some cases, studies have been conducted on exhumed bodies to detect the presence of drugs or toxins, enabling the determination of the time interval during which these substances were present in the human body [10,11].

The research conducted in the previous decade has focused on various investigative procedures related to different drugs of abuse and their metabolites, utilizing diverse biological samples such as saliva, blood, and hair. Several countries are currently exploring and analyzing alternative samples for drug testing, moving beyond traditional samples like urine or blood. Hair and nail analysis, proven to be effective in the treatment of drug addicts, has also played a crucial role in solving drug-facilitated crimes such as rape cases and child sexual abuse cases.

Hair analysis initially emerged during the 1960s to 1970s for investigating heavy metal poisoning using atomic absorption spectrometry. Subsequent extensive research on hair analysis during the 1970s and 1980s primarily focused on heroin addicts. Presently, the most commonly employed method for analyzing drug abuse in addicts' hair is GC-MS. Many researchers consider hair and nails as optimal sources for drug and toxin analysis due to their longer inspection window compared to other biological fluids from the human body.

The field of toxicology and hair/nail analysis has witnessed significant advancements in instrumentation over time, driven by researchers' pursuit of improved analytical technology and the need for more accurate and sensitive detection methods. Initially, Gas chromatography (GC) was the primary method utilized. In the 1970s and 1980s, GC was coupled with a Flame ionization detector (FID) and widely acclaimed for drug analysis in hair and nails. Subsequently, atomic absorption spectrometry emerged as a technique for hair analysis, particularly in the investigation of heavy metal poisoning. In the 1970s, Gas chromatography – Mass spectrometry (GC-MS) revolutionized the field of analytical toxicology, enabling the identification and quantification of drugs in hair analysis. During the 1980s, Liquid chromatography (LC) came into existence, gaining prominence as High-Performance Liquid Chromatography (HPLC) due to its ability to analyze non-volatile and polar compounds.

Later, in the 1990s and 2000s, LC was combined with mass spectrometry, providing a broader range of compound analyses, including polar and non-polar compounds. As technology continued to evolve, different instrumentation techniques such as Inductively Coupled Plasma-Mass Spectrometry (ICP-MS), Fourier Transform Infrared Spectroscopy (FTIR), and X-ray Fluorescence (XRF) were developed and utilized in the field of toxicology for hair and nail analysis.

Analytical toxicology of human hair has witnessed significant advancements in recent years, enabling more precise and comprehensive assessments of exposure to drugs, chemicals, and other toxic substances. One key area of progress is biomonitoring, where hair and nails have been recognized as valuable matrices for evaluating individuals' exposure to environmental chemicals and contaminants. The use of an atomic absorption spectrometer allows for the detection of heavy metals like lead and cadmium in these samples.

In forensic drug testing, hair and nails are frequently employed to demonstrate long-term drug consumption. Hair is particularly suitable for detecting most basic chemicals, while nails are effective for neutral and weakly acidic substances. Hair and nails also serve as indicators of chronic exposure to environmental toxins, including industrial chemicals, heavy metals, and persistent

organic pollutants. An intriguing study on chlorinated paraffin (CPF) exposure revealed that CPF levels increase proportionally to individuals' age. This finding suggests that the accumulation of chlorinated paraffin in hair and nails may primarily depend on a person's age and in turn reflect the duration of exposure.

In the field of forensic toxicology, hair, and nails have emerged as valuable sources of evidence. Analytical techniques have been refined to identify various chemicals in these matrices, including pharmaceuticals, toxins, and poisons. Moreover, isotopic analysis of hair can unveil information about a person's geographic origin and travel history, aiding in forensic geo-profiling. Hair and nails also offer insights into occupational exposure to harmful chemicals. Researchers have investigated the connection between workplace exposure and the accumulation of toxins in these matrices, providing valuable information for assessing occupational health hazards. The advancements in the analytical toxicology of hair and nails have enhanced our ability to assess exposure to drugs, chemicals, and toxins, contributing to various fields such as biomonitoring, forensic science, and occupational health. These developments continue to improve our understanding of human exposure and aid in the detection and prevention of potential health risks [12,13].

The advent of high-resolution mass spectrometry has brought about a revolutionary change in hair analysis, enabling the detection and quantification of a broad range of compounds even at exceptionally low concentrations. Baumgartner et al. (2021) developed an overly sensitive and reliable method using ultra-high-performance liquid chromatography coupled with tandem mass spectrometry (UHPLC-MS/MS) to simultaneously determine opioids, stimulants, benzodiazepines, and new psychoactive substances (NPS) in hair samples. Salomone et al. (2020) provided a comprehensive overview of recent advancements in hair analysis for detecting drugs of abuse, including improvements in sample preparation techniques. Kim et al. (2020) demonstrated the application of direct analysis in real-time-high-resolution mass spectrometry (DART-HRMS) for rapid screening and identification of drugs and their metabolites in hair samples. This approach allows for the simultaneous detection of multiple chemicals without the need for lengthy sample preparation [14-17].

Segmental analysis is the process of examining various sections of hair to identify the pattern of exposure over time, which can reveal crucial details regarding the frequency and severity of the exposure. Micro Segmental Hair Analysis (MSA), which removes individual hair strands at intervals of 0.4 mm, or roughly one day's worth of hair development, was created in 2016. This technique provides thorough information regarding the process of drug intake into hair as well as strong proof of drug use in investigations of drug-related crimes [18].

The isotopic composition of elements in a hair sample can be determined using Isotopic Ratio Mass Spectrometry (IRMS), which can provide information about the person's geographic origin and the substances to which they have been exposed. This method has enormous potential for use in forensic investigations as well as studies on environmental exposure.

Hair analysis has been used to uncover metabolic fingerprints connected to drug or chemical exposure through the study of tiny molecules (metabolites) produced by cells and tissues, or Metabolomics. This method can offer a more thorough and in-depth evaluation of exposure as well as insight into the toxicity mechanism. Hair possesses enormous potential as a

metabolomic sample for monitoring chronic diseases. A study was conducted aiming to investigate the metabolic alterations in hair to elucidate a suitable treatment modality for Methamphetamine use disorder. Consequently, hair samples taken from current and previous methamphetamine use disorder patients underwent both targeted and untargeted metabolomics analysis using mass spectrometry. A similar approach can be practiced in conducting research on exposure to other drugs of abuse [19].

We can now detect and quantify drug and toxic substance exposure, as well as comprehend the long-term implications of this exposure on human health, thanks to advancements in the analytical toxicology of human hair. In the upcoming years, these techniques are probably going to keep developing and getting better, giving us new perspectives on the intricate connection between environmental exposure and human health [20].

A current field of study in the toxicology of human hair and nails is the identification of new pharmacological targets. Recent research has concentrated on finding new psychoactive compounds (NPS) in hair, nails, and other body tissues. Examples of NPS include synthetic cannabinoids and cathinones. The importance of detecting NPS in hair and nails has grown because of their pervasiveness in the drug market and their possible health dangers. Depending on the length of the hair & nail sample taken, drug and toxin testing is a viable approach for identifying drug usage over an extended period of time, which can range from weeks to months or even years [21,22].

The general timeline for finding drugs in human hair & nails is summarized in Table 1.

Table 1. Detection of Drugs in Hair and Nails [22,23,24]

S.No.	DRUG/TOXIN	Metabolites	Minimum Detectable Levels	In Hair	In Nails
1.	Cocaine	Benzoylecgonine and ecgonine methyl ester	0.5 ng/mg	Up to 90 days after use	up to 6 months after consumption
2.	Marijuana	11-Nor-9-carboxy-delta-9-tetrahydrocannabinol (C-THC)	0.1 ng/mg	Up to 90 days after use	up to 6 months after consumption
3.	Opioids	Monoacetylmorphine, Morphine, Codeine	0.2 ng/mg	Up to 90 days after use	up to 6 months after consumption
		2- ethylidene- 1,5-dimethyl-3,3-diphenylpyrrolidine, (EDDP)	0.5 ng/mg		
4.	Amphetamines	Methylenedioxyamphetamine	Hair- 8.0ng/mg Nails-9.7ng/mg	Up to 90 days after use	

	E.g.: Methamphetamine and Adderall	3,4 methylenedioxymethamphetamine	Hair-53.4ng/mg Nails-60.2ng/mg		up to 6 months after consumption
5.	Benzodiazepines (such as Xanax and Valium)/ Non benzodiazepine hypnotics/ Antidepressants etc.	Venlafaxine	Hair-44.31 ng/mg Nails-7.02 to 22.6 ng/mg	Up to 90 days after use	up to 6 months after consumption
		Zolpidem	Hair-0.16ng/mg Nails-0.40 to 1.42ng/mg		
6.	Alcohol or its metabolites	Ethyl glucuronide (EtG)	Hair-2.1 to 3.5 pg/mg Nails-2.3 to 23 pg/mg	Several months after consumption	up to 6 months after consumption
7.	Heavy metals such as Lead, Mercury Etc.	Depends on the type of heavy metal poisoning.	Variable based on techniques used	Up to 12 months after intake	up to 12 months after consumption

It is important to note that hair drug testing has a longer detection window than urine or blood testing for drug use. This is because when hair grows, drugs and their metabolites get trapped in the shaft, extending the detection window. Human nail drug testing can offer a wider detection window than hair drug testing. Since nails grow more slowly than hair does, and nails are four times thicker than the typical strand of hair and often capture more substances than hair can, drugs and their metabolites get more deeply impregnated and are therefore more detectable for longer periods. But one must consider that the detection window can change depending upon several factors including the user's rate of hair and nail growth, the dosage, exposure, and strength of the drug, and the accuracy of the test results which can also be impacted by hair treatments, nail polishing, use of cosmetics and also coloring of nails and hair [25].

Due to their toxic effects on hair follicles, poisonings brought on by substances like arsenic, thallium, and heavy metals can result in alopecia. For instance, arsenic interferes with the cellular processes necessary for hair growth and can cause premature hair loss. The production of keratin, a protein necessary for the growth of new hair, is inhibited by thallium poisoning, which causes hair loss. Additionally, cancer chemotherapy is also a cause of alopecia. In such cases, it is difficult to obtain hair samples for analysis. Several nail pathologies can impede the utility of nails for toxicology purposes. Onychomycosis, psoriasis, and chronic paronychia can induce structural abnormalities, thereby hindering the acquisition of dependable samples for toxicological analysis. Furthermore, significant nail trauma, such as nail bed lacerations or extensive nail matrix impairment, can compromise the nail's integrity, thereby impacting its suitability for toxicology testing.

To guarantee the accuracy and reproducibility of the results, validation, and standardization of hair and nail analysis methodologies are essential. The quality

control and inter-laboratory comparability of the results have been enhanced with the establishment of standardized protocols and guidelines for hair and nail analysis, such as those from the Society of Hair Testing and the Society of Forensic Toxicologists.

The creation of novel analytical methods and the fusion of various OMICS approaches will determine the future direction of human hair and nail toxicology studies for medico-legal purposes. It is anticipated that improvements in metabolomics and imaging mass spectrometry will help find new biomarkers for drug exposure and give spatially resolved data on drug distribution in hair and nails. [26].

The application of Forensic tricho-toxicology and Forensic onycho-toxicology in Forensic Medicine is as follows:

1. Hair and nail samples are of utmost importance in cases of an autopsy upon exhumation to rule out heavy metal criminal poisoning. A routine practice of collecting these specimens for chemical analysis should be considered in all exhumation cases where it is felt necessary.
2. Substance abuse assessment in living and dead, especially in cases of drug-facilitated acute/chronic sexual assault/abuse. This shall become crucial evidence if the timing of exposure to drugs could be ascertained with certainty.
3. Occupational exposure assessment to various industrial toxins in both the living and the dead. This has a wide range of occupational safety and health applications and aids in the process of establishing a temporospatial association between the toxin and disease.
4. Environmental exposure assessment to various toxins can be easily identified by using nails and hair as substrates. This has an application in forensic medicine in investigating chronic accidental poisoning as a cause of death.
5. The toxicological analysis of hair and nails may provide drug abuse-related insights into investigating sudden deaths in young individuals, where no other cause is apparent at autopsy.
6. Autopsy surgeons may also consider the role of hair and nails as routine samples for chemical analysis to identify the cause of death in poisoning cases.
7. The forensic taphonomy study of hair and nails may also provide insights into antemortem exposure to various toxic substances.
8. The cause of death due to chronic damage caused by antipsychotics/antidepressants amongst psychiatric patients can be ascertained using the toxicology of hair and nails.
9. In all cases where a corpse is found in an advanced state of decomposition, it is advisable to preserve hair and nails for chemical analysis as a matter of routine because they constitute a relatively fresh sample for analysis even days after death.

The toxicology of hair and nails may also provide further insights into therapeutic drug monitoring and chronic disease management in the future.

It is also pertinent to mention that over-interpretation of the toxicology of hair and nail data can sometimes make us miss the forest for the trees. An autopsy surgeon should cautiously interpret these results in accordance with the objectives of a medico-legal autopsy.

Conclusion

In conclusion, the field of toxicological investigation utilizing human hair and nails as substrates is rapidly advancing. Recent developments in sampling and preparation techniques, as well as our understanding of drug metabolism and disposition, identifying new therapeutic targets, and establishing validation and standardization protocols have greatly improved the reliability and reproducibility of results.

Future research efforts are expected to focus on several areas to enhance the utility of hair and nail analysis in forensic toxicology. Firstly, the development of innovative analytical methods will be crucial in expanding the range of detectable substances and improving sensitivity and specificity. Additionally, incorporating OMICS methodologies, such as genomics, proteomics, and metabolomics, into hair and nail analysis holds promise for gaining a deeper understanding of drug exposure, metabolism, and individual variations.

These advancements will contribute to the continued growth and application of hair and nail analysis in forensic toxicology, enabling forensic scientists and practitioners to obtain valuable information on drug use, exposure to toxins, and other relevant factors. As research progresses, the field will continue to evolve, providing even more accurate and comprehensive insights into forensic investigations and contributing to the advancement of forensic medicine.

Conflicts of interest

The authors declares that they do not have conflict of interest.

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CASE REPORT

A Documented case of a Horseshoe kidney with Pelvi-ureteric junction obstruction due to high insertion of the ureter

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Abstract

Horseshoe kidney is the most common genitourinary tract fusion abnormality at a frequency of 1 in 400-800 live births. PUJ obstruction is observed in up to one-third of these cases. The clinical presentation of the patients present will be either asymptomatic or may include stomach discomfort, persistent UTIs, and calculi. The PUJ obstruction is managed by surgery which can be carried out using a robotic, laparoscopic, or open technique. We hereby present a case of 16 hear old female with right sided PUJ obstruction due to high ureteric insertion in a horseshoe kidney which was effectively managed by open Anderson-Hynes Pyeloplasty.

Keywords: High ureteric insertion, horseshoe kidney, PUJ obstruction, pyeloplasty

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Introduction

The most prevalent kidney fusion anomaly is the horseshoe kidney (HSK), which affects about 0.25% of the general population. The male to female ratio for the occurrence of horseshoe kidney is 2:1 [1]. There is frequent occurrence of PUJ obstruction in horseshoe kidney. [1] Renal malrotation, fluctuating blood supply, high ureteric insertion lead to a high susceptibility to develop Pelvi-ureteric junction (PUJ) obstruction in up to one third of cases [2]. We hereby report a case of PUJ obstruction in horseshoe kidney in a 16-year-old female which was caused due to high ureteric insertion.

Case Presentation

A 16 hear old female presented to the urology outpatient department with lower abdominal pain sine 1 month. The pain was intermittent and colicky in nature and not associated with any febrile episodes or haematuria. Patient was further evaluated using biochemical parameters which revealed normal creatinine of 0.58 mg/dl and normal white blood cell count. She underwent ultrasound which revealed a HSK with right sided hydronephrosis. A Computerised Topography-Intravenous Urography (CT-IVP) revealed horseshoe kidney with the lower poles of bilateral kidneys fused at lower end of body of L3 vertebra with the right segment of the horseshoe kidney showing hydronephrosis with obstruction at pelvi-ureteric junction. The left kidney was normal in enhancement and excretory function (Figures 1-3).

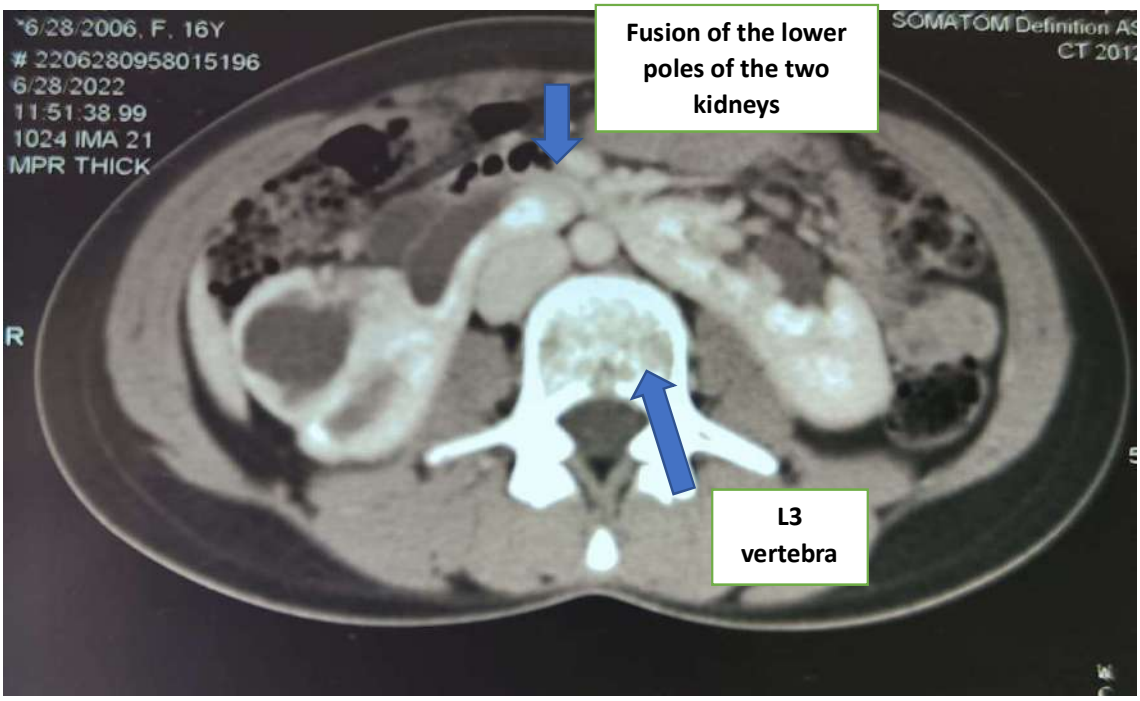

Figure 1. Axial section of CT-IVP images showing right sided hydronephrosis and the isthmus of the horseshoe kidney.

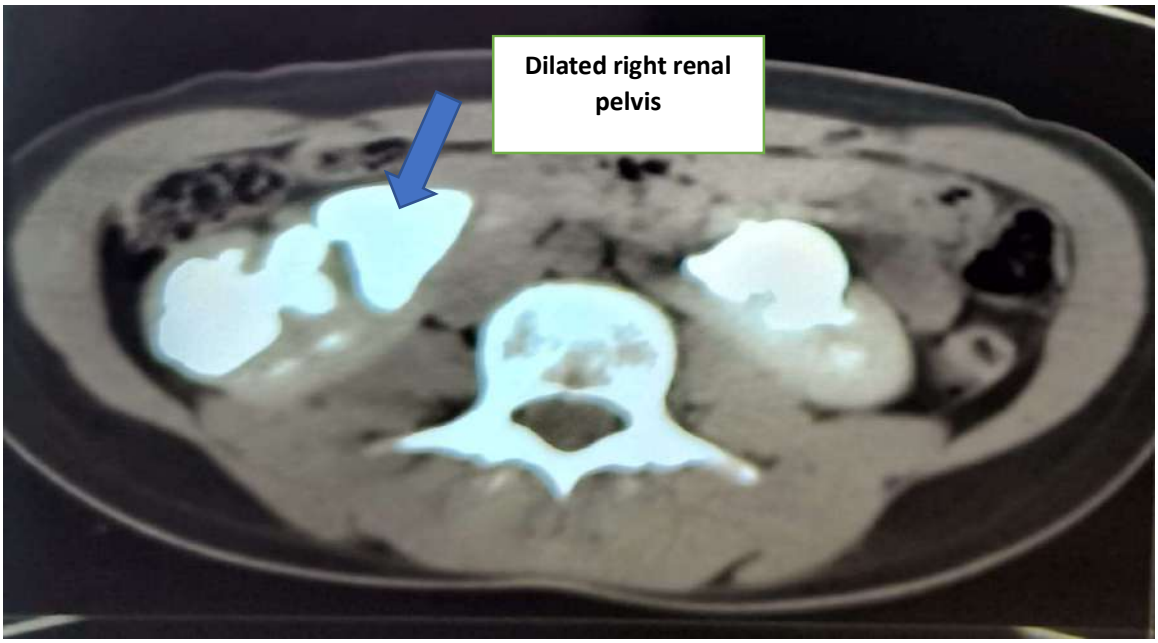

Figure 2. Axial section of excretory phase of CT-IVP showing right sided hydronephrosis and dilated right renal pelvis till the level of right PUJ.

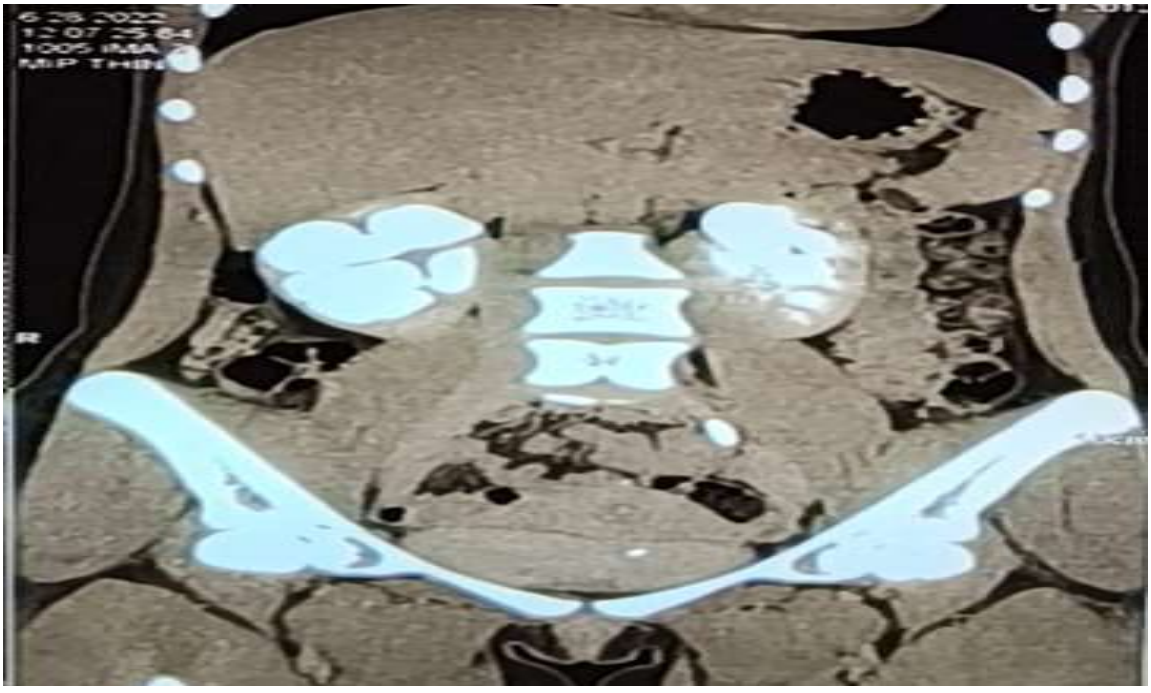

Figure 3. Coronal section of CT-IVP showing Grossly dilated right sided Pelvi-calyceal system till the level of Right PUJ

Patient was further evaluated with T-99 DTPA scan-F+0 protocol to determine the differential function of the two segments of the HSK. The right segment of the HSK showed type 2 O-Reilly curve with differential GFR of 28.9 ml/min (37%) with left segment showing normal enhancement and excretory function with differential function of 49.4 ml/min (63%) (Figure 4).

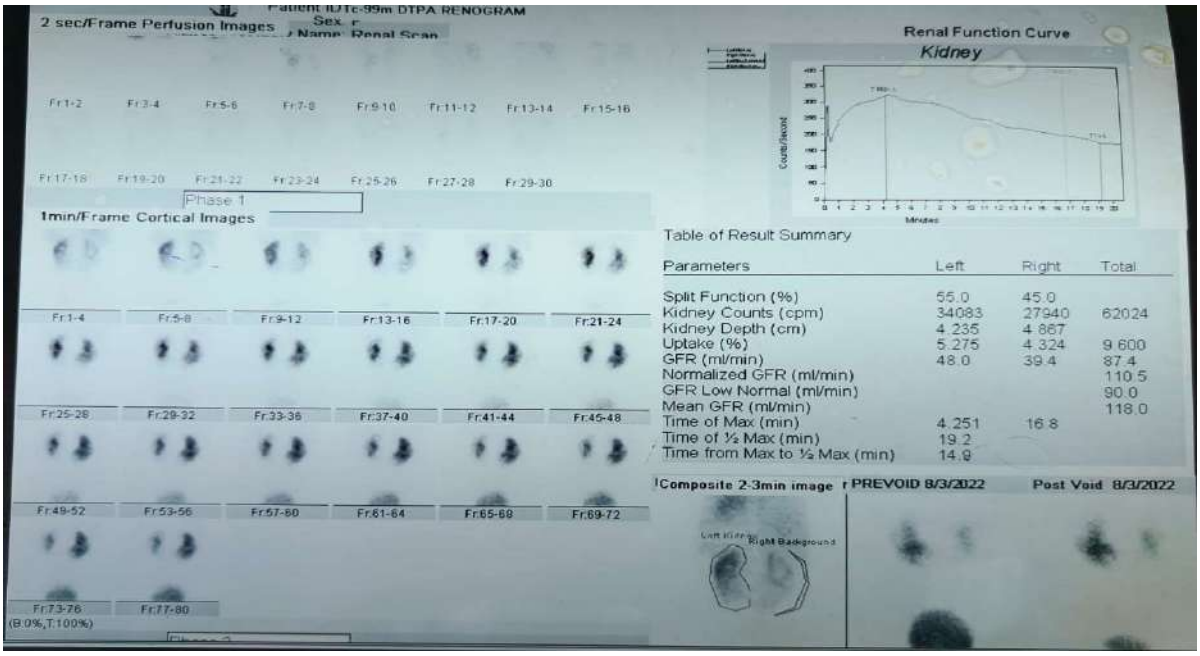

Figure 4. DTPA scan showing type 2 O-Reilly curve for the right kidney indicating obstructive drainage on the right side.

Hence, the patient was planned for open right sided Pyeloplasty. Through a lower midline vertical incision, the right segment of the horseshoe kidney was exposed along with the PUJ and the site of the obstruction. It revealed high insertion of the ureter being the cause of the obstruction. This was tackled using Modified Anderson Hynes Pyeloplasty to form a dependent funnel-shaped tension free anastomosis using 3-0 polydioxanone (PDS) suture with placement of 6/24 DJ stent (Figures 5-7). The incision was closed after placement of a pelvic drain. The patient was discharged after 5 days of admission in the hospital after removal of foley catheter and pelvic drain with a uneventful postoperative recovery.

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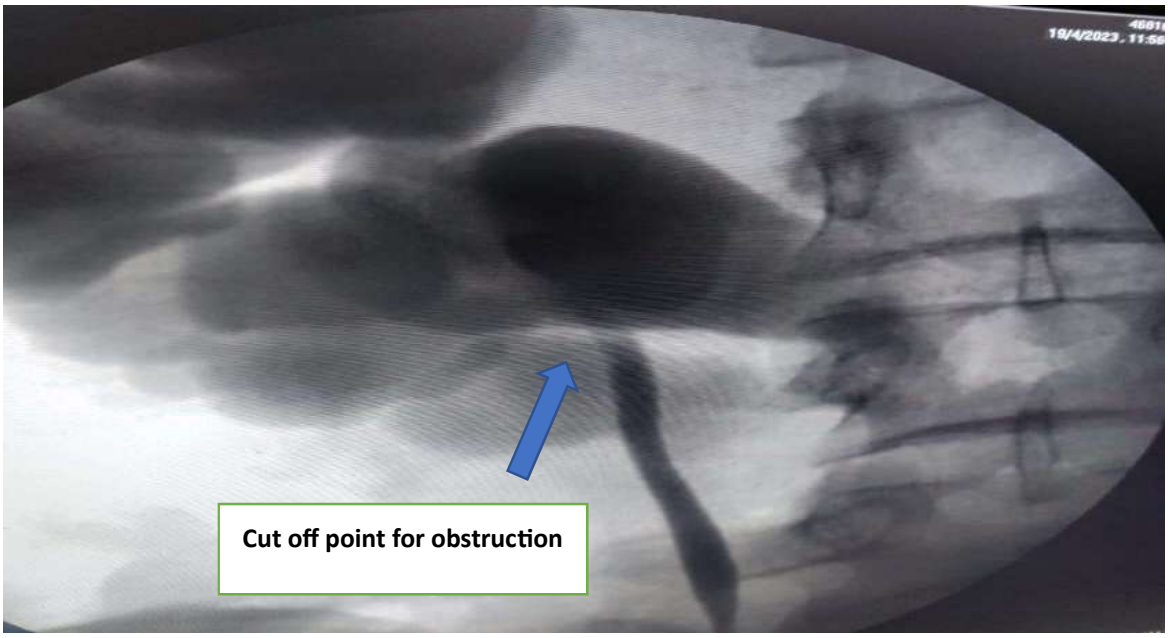

Figure 5. Right side Retrograde pyelography showing PUJ obstruction.

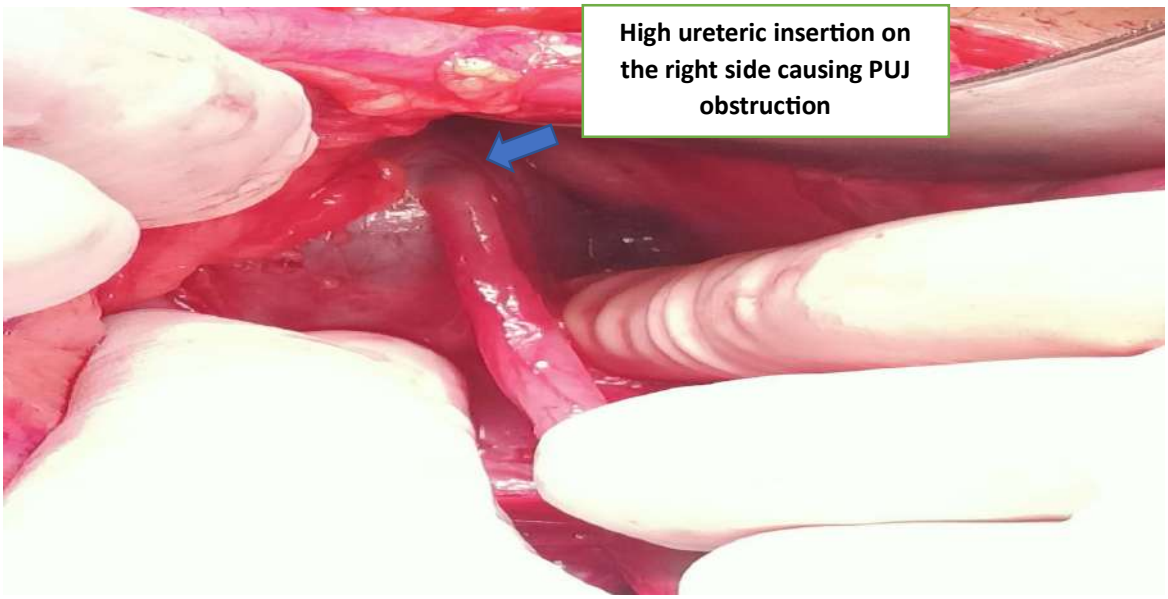

Figure 6. Intraoperative image showing high ureteric insertion on the right side causing PUJ obstruction.

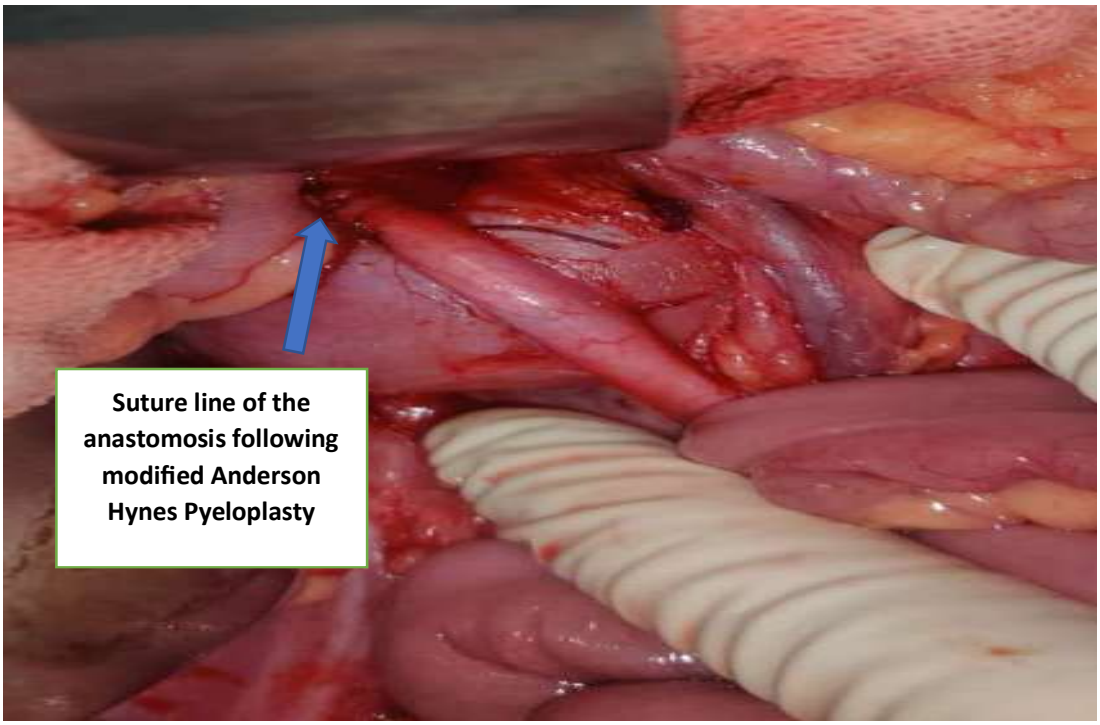

Figure 7. Intraoperative image of the Suture line following Modified Anderson Hynes Pyeloplasty using PDS 3-0.

The DJ stent was removed 6 weeks after the surgery and a retrograde pyelography performed at this stage revealed prompt excretion of contrast of the right sided pelvi-calyceal system. A DTPA scan at 3 months revealed relief of obstruction and good excretion of contrast with a normal excretory curve. Patient was last followed up at 6 months and has not reported any complaints and has been doing well.

Discussion

Horseshoe kidney is the most prevalent kidney fusion anomaly, which affects 0.25% of the general population [3]. The period between 4 and 8 weeks of development when the metanephric buds fuse, which prevents their normal rotation and cephalic migration results in this congenital abnormality [3]. The anterior location of hydronephrosis is frequently caused by the horseshoe kidney's renal pelvis and ureters, which have a propensity to kink and lie anterior to the isthmus [4]. Congenital stricture, high ureteral insertion, an irregular ureteral course through the isthmus, crossing vessels supplying the isthmus, or aberrant motility of the PUJ segment are all hypothesised to contribute to PUJ obstruction [5]. Hydronephrosis from PUJO occurs in about 14% to 35% of cases of horse shoe kidney [6,7]. The different presentation of the patients are those of infection, calculi, obstruction or tumour due to the abnormal anatomy. Urolithiasis and PUJ blockage are the two most frequent complications of the horseshoe kidney that require surgical intervention, with an incidence of 20–60% and 15–33%, respectively [8]. Preoperative imaging helps to assess the anatomical abnormalities one will encounter during the surgery. The basic surgical principles of management are excision of stenotic ureteropelvic segments, excision and refashioning of a redundant pelvis, transposition of aberrant vessels if any and a dependent water-tight

funnel-shaped ureteropelvic anastomosis [3]. Dismembered pyeloplasty is an effective treatment for horseshoe PUJ blockage brought on by an intrinsic stenosis, high ureteral insertion, or an irregular course of the ureter across the isthmus. The procedure of choice for treating PUJO in HSK is dismembered pyeloplasty [9]. The different approaches include trans-peritoneal approach by a lower midline or transverse incision or by the retroperitoneal approach via a flank incision provide excellent exposure of the PUJ in horse shoe kidneys [3,9]. The success rates following Anderson-Hynes pyeloplasty in horseshoe kidneys are equivalent to those in hydronephrotic kidneys that are located properly [9]. On the other side, the Foley Y-V plasty has a success rate that is close to 80% [7]. A vascular hitch or dismembered pyeloplasty can be used to treat a crossing vessel causing PUJ obstruction. A bigger number of sample size of case series will be required to establish guidelines for this condition but however, given the rarity of the condition, such studies are not available.

In our case, it reaffirms the fact that modified for the treatment of PUJ obstruction in HSK kidney, Anderson-Hynes pyeloplasty without extra division of the kidney's isthmus is a highly effective technique.

Conclusion

Thus, our case report affirms that adequate preoperative imaging is needed to evaluate the abnormal anatomy in case of horseshoe kidney and that PUJ obstruction in horseshoe kidney due to high insertion of ureter can be effectively managed by Modified Anderson-Hynes pyeloplasty.

Conflicts of interest

The authors declares that they do not have conflict of interest.

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CASE REPORT

Rapunzel Syndrome: The not-so-fairy tale of a long tail

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Abstract:

Background: Rapunzel Syndrome associated with Trichobezoar secondary to a psychiatric illness Trichotillomania, is often a rare diagnosis of Gastrointestinal symptoms, occurring predominantly in young & adolescent females.

Clinical Description: We present here a case of such disease in a 12-year-old female who presented to us with recurrent vomiting & pain abdomen for the last 2 months.

Management & Outcome: On thorough examination & investigations, she was suspected to be a case of trichobezoar on ultrasound abdomen, which was confirmed by upper GI endoscopy. Mass was surgically removed from the patient's abdomen with a long tail of Rapunzel.

Conclusion: Although trichobezoar is a rare condition, it must be considered in patients with trichotillophagia & abdominal symptoms. Symptomatic trichobezoars are often so large that they are palpable on simple clinical examination as in this case. USG may be inconclusive and endoscopy is confirmative. Undiagnosed or untreated trichobezoar continues to grow in size & weight, resulting in devastating complications, such as gastric ulcers, perforation, or even death.

Keywords: Trichobezoar; Trichotillomania; trichotillophagia; Rapunzel Syndrome

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Introduction

Indigestible accumulation of foreign material in the gastrointestinal tract is called 'bezoar'. The collection of fibers or plants is called 'Phytobezoar', collection of milk is 'Lactobezoars', collection of hairs is termed as 'Trichobezoar' & collection of medication is 'Pharmacobezor' [1]. Trichobezoar is more common in young girls & results due to psychiatric conditions like 'trichotillomania' (hair pulling) & 'trichophagia' (hair swallowing). A rare & unusual presentation of trichobezoar is when hairs extend into the intestines from the stomach & this condition is called as Rapunzel Syndrome. Removal by using an endoscope may be possible for small trichobezoars while large ones need surgical intervention [2]. Here, we report a case of Rapunzel Syndrome in which the mass was removed surgically.

Case Report

A 12-year-old female child weighing 27 kg presented to Out Patient Department of our hospital with complaints of pain abdomen for the last 2 to 3 months, which was insidious in onset, mainly in the epigastric region, with no radiation, mild to moderate in intensity, no diurnal variation, occasionally colicky in nature with no aggravating or relieving factors. She also had a history of vomiting for the last 2 to 3 months, mostly after ingestion of food, approximately 3-5 episodes per day, non–bilious in nature, projectile and mainly containing food particles. There was no history of fever, headache, constipation, or abdominal distension.

General examination revealed pallor. On per abdomen examination, there was an intra-abdominal mass palpable in the epigastric region extending up to the left hypochondrium which was approximately 5x5 cm in size, round in shape, with smooth surface, well-defined margins with normal skin overlying the mass, firm in consistency, non-tender, moving with respiration, non-pulsatile, non-fluctuant, non-reducible or compressible, non-trans-illuminant & non-pitting on pressure. There was no hepatosplenomegaly. Initially, a differential diagnosis of malignancy was thought of.

The patient was admitted to Pediatric Intensive Care Unit and a workup was done, which revealed Hb- 9.2 gm/dL %; TLC- 9,420/µL; DLC- $N_{67}L_{22}$; PLT- 2.79 lacs/µL; MCV-78.5 fl; MCH- 23.2 pg; RDW–14.5%; Reticulocyte Count – 2.6%; S. Creatinine- 0.66 mg/dL; B. Urea – 30 mg/dL; Na – 130 mEq/L; K- 3.3 mEq/L; OT/PT – 47/24 Units/L; Total Bilirubin- 0.28 mg/dL.

Ultrasound abdomen revealed an echogenic lesion with posterior acoustic shadowing of size approximately 68 x 62mm in the left hypochondriac region, with a possibility of Trichobezoar.

History was reviewed and a history of Trichotillomania and Trichophagia for the last 2 years was elicited due to which parents trimmed her hair.

Trichobezoar of about 10 x 15 cm was confirmed on Upper GI endoscopy and surgery was planned after clearing the pre-anesthetic checkup.

A midline incision was given over the epigastric region, planes were dissected, the anterior stomach wall was opened, trichobezoar was identified & was extracted along with the tail of Rapunzel of about 50 cm, extending up to jejunum (Figure 1). The stomach was then closed &

skin sutures were finally placed thus completing the surgery. The patient was subsequently kept nil per oral, along with intravenous fluids and antibiotics. She recovered well. Feeds were started on the 7th day and the patient was discharged on post-operative day 10. A psychiatry reference was done subsequently.

Discussion

Accumulation of exogenous matter in the stomach or intestine, is called a bezoar which is predominantly composed of food & fiber. The term 'bezoar' is derived from the Arabic word 'badzehr' which means antidote [1]. Females with underlying personality disorders or neurologically impaired persons are more prone to develop bezoar. Apart from this, patients who have undergone abdominal surgery are also at higher risk of developing bezoars, as it decreases the size of the stomach, interferes with the passage of gastric contents and leads to reduced secretion of gastric acid [3]. Diabetes mellitus, autoimmune diseases, peptic ulcer disease, Crohn's disease, carcinoma of the GI tract, hypothyroidism & excessive fiber intake are some of the other predisposing factors for bezoar formation [4]. The peak age of onset of symptoms is 2nd decade of life [5].

Trichotillomania, a psychiatric condition, is most frequently associated with this condition and the most severe form is known as Rapunzel syndrome (hair bezoar extending beyond the stomach to the small intestine).[6] It is named after a tale written in 1812 by the Brothers Grimm, about a long-haired young maiden, Rapunzel, who lowered her hair to the ground from a castle in order to permit her young prince to climb up [7]. Rapunzel Syndrome was described for the first time in 1968 by Vaughan et el., and it is almost exclusively seen in young females [8].

Phytobezoars are composed of a combination of plant & animal material. Lactobezoars were previously found most often in premature infants & can be attributed to the high casein or calcium content of some premature formulas. Swallowed chewing gums can occasionally lead to a bezoar.

Symptoms of gastric outlet or partial intestinal obstruction, including vomiting, anorexia, & weight loss are the main manifestations of trichobezoar. Complaints of abdominal pain, distension and severe halitosis, with physical examination demonstrating patchy baldness & a firm mass in the left upper quadrant are characteristics of trichobezoar [9]. Patients occasionally have iron deficiency anemia, hypoproteinemia, or steatorrhea caused by associated chronic gastritis.

An abdominal plain film suggests the presence of bezoar, which can be confirmed by ultrasound or CT examination which show a nonhomogeneous, non-enhancing mass within the lumen of the stomach or intestine [4].

Bezoars in the stomach can usually be removed endoscopically if they are of small size & confined to the stomach only with no satellite masses. Lactobezoars usually resolve when feeding is withheld for 24-48 hrs. Coca-Cola has been used as a dissolution therapy for gastric phytobezoar & has been shown to be effective when used with endoscopy [10].

Sunflower seed bezoars are reported to cause rectal pain & constipation as a result of seed shells being associated with fecal impaction [11]. Endoscopic removal is indicated, as these bezoars are refractory

to enema or lavage management. Trichobezoars almost always require surgical removal as in our case.

Conclusion

Although trichobezoar is a rare condition, it must be considered in patients with trichotillophagia & abdominal symptoms. Symptomatic trichobezoars are often so large that they are palpable on simple clinical examination as in this case. USG may be inconclusive and endoscopy is confirmative. Undiagnosed or untreated trichobezoar continues to grow in size & weight, resulting in devastating complications, such as gastric ulcers, perforation, or even death.

Conflicts of interest

The authors declares that they do not have conflict of interest.

Author contibution

All authors have equal contributions to patient care, establishing a clinical diagnosis, planning investigations, management and follow-up. Dr. Deepak Mittal was the chief Operating Pediatric surgeon. All have contributed to manuscript preparation.

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CASE REPORT

Tuberculous mesenteric cyst of the small intestine in a 16-year-old male without history of abdominal tuberculosis: A rare presentation

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Abstract
One mesenteric cyst in every 250,000 admissions to a hospital is a benign intra-abdominal tumor. We report a 16 year old male who came to our outpatient department with complaints of vague pain in the abdomen. Imaging revealed it as mucinous cystic neoplasm, infected mesenteric cyst or hydatid cyst. Diagnostic laparoscopy was performed and it confirmed the cyst originating from mesentery, as they were huge, laparotomy was performed. Following which the histopathologic report was different from what was expected, it was reported as an tuberculous mesenteric cyst. Following recovery patient was referred to infectious diseases specialist and was started on Anti Tuberculous Treatment.

Keywords: Mesenteric cyst, mucinous cystic neoplasm, infected mesenteric cyst, hydatid cyst, surgery, tuberculous cyst

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Introduction

Mesenteric cyst are rare benign intra-abdominal tumors with an incidence of 1 case per 250,000 hospital admissions [1]. During an abdominal radiological examination, they are discovered accidentally due to their non-specific and variable clinical signs and symptoms. These cysts have no known etiology, but there are a few theories about how they develop. Complete careful extraction of the cyst is the treatment of choice. Correct preoperative diagnosis is difficult due to its rarity and lack of specific symptoms. Due to the numerous complications that result from poor surgical management, having knowledge of these lesions is essential.

Case Report

A 16 year old male, native of Assam presented to our outpatient department with complaints of global vague abdominal pain of 6 months duration, particularly postprandial, not associated with fever, chills, cough, loss appetite, loss of weight, hematemesis, melena, jaundice. No significant family history was mentioned. On examining the patient, he was well built, with stable vital signs, anicteric. On examining the abdomen, two well- defined oval shaped, intra abdominal lump, one lump with the left hypochondrium and other lump confined within the right iliac fossa, non tender on palpation, with well defined margins. It was mobile from side to side. His laboratory values were all within the normal range. Chest X Ray was unremarkable, Ultrasound whole abdomen revealed an intra- abdominal cystic masses within the left hypochondrium and right iliac fossa. Based on the features on the ultrasonography “Mesenteric Cyst” was diagnosed provisionally. CECT Abdomen was contemplated along with ultrasonography, which revealed Thick walled multiloculated complex mesenteric cystic lesion seen in the right abdomen abuting the iliocolic artery, and left abdomen abbuting the firts jejunal branch of superior mesenteric artery? mucinous cystic neoplasm? infected mesenteric cyst? hydatid cyst (Figure 1). Therefore, patient was prepared for Diagnostic laparoscopy and proceed, a 5mm laparoscope was placed in the palmer’s point, revealed 2 huge cystic lesions and no other significant pathology within the abdominal cavity, another 5mm left lumbar port placed for manipulating the bowel, which confirmed cystic lesion arising from mesentery, as the cystic lesions were huge, exploratory laparotomy was performed, it revealed an hard cystic lesion approximately 8* 5cm within the jejunal mesentery along the first jejunal artery, 15 cm from the DJ flexure, another cystic lesion observed within the ileal mesentery abuting the iliocolic artery approximately 10*6 cm and 20 cm from the ileocecal junction (Figure 2).

Careful dissection was performed protecting the vasculature of the small bowel, the proximal mesenteric cyst as was completely occluding the first jejunal artery hence it was decided to go along with bowel resection of, involved segment followed by side to side Jejuojujunal anastomosis, the distal mesenteric cyst came out en block without affecting the ileocolic artery. Following excision of the cyst, the mesenteric rents were closed to prevent internal hernia. Patient tolerated the

procedure well and recovered without any untoward events. Histopathology examination showed sections of matted lymph nodes and parinodal soft tissue and mesenteric tissue with numerous epitheloid granulomas with multinucleated gaint cells and extensive areas of necrosis. Sinus tract is also seen from the overlying mesothelium. Stains for fungus and AFB Tb are negative an impression of MESENTERIC CYST with lymph nodal and mesenteric tissue with necrotizing granulomatous inflammation with sinus tract formation and mesenteritis (Figure 3). Gene Xpert MTB of the cyst contents were positive to Mycobacterium Tuberuloisis, following which patient was discharged on Post Op Day 5 and was advised to undergo Anti Tuberculous Treatment and with regular follow up.

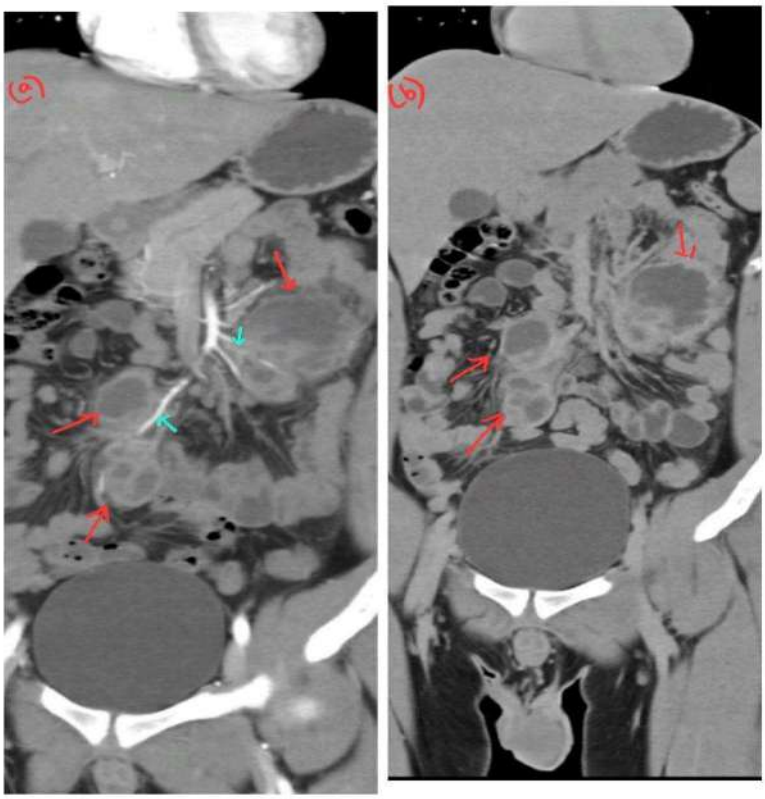

Figure 1. **a)** Contrast enhanced CT abdomen showing 7*5*4 cm multiloculated cystic mesenteric lesion, with thick septations on left side of abdomen (red arrow on left), the jejunal branches of the superior mesenteric artery being involved (blue arrow on left). 7*4*3.5 cm multiloculated mesenteric cyst on the right side of the abdomen (red arrows on right), the cystic lesion is saddling the ileocolic branch of the superior mesenteric artery. **b)** CT abdomen without contrast.

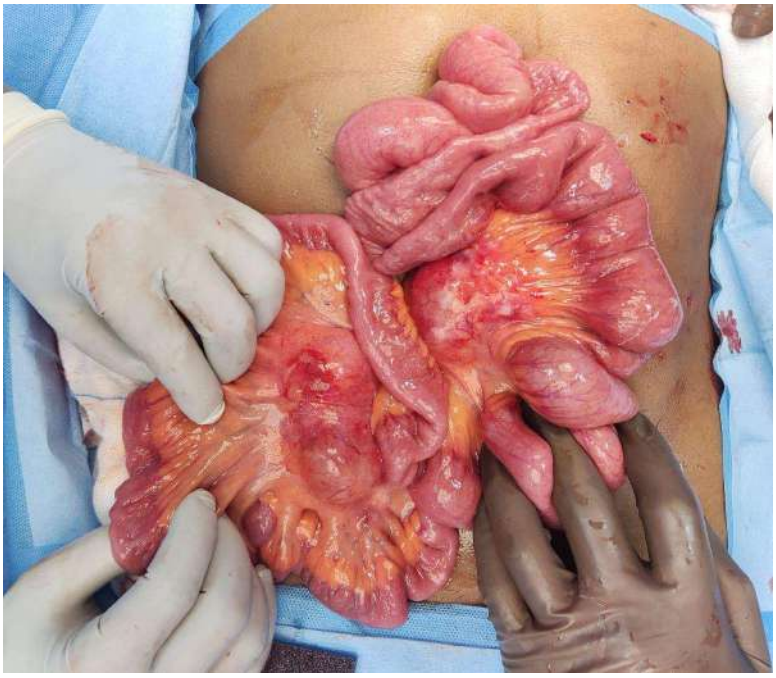

Figure 2. Intraoperative picture of the above said findings, left sided mesenteric cyst was 20cm from the DJ flexure, the right sided mesenteric cyst was 25 cm from the ileocecal valve.

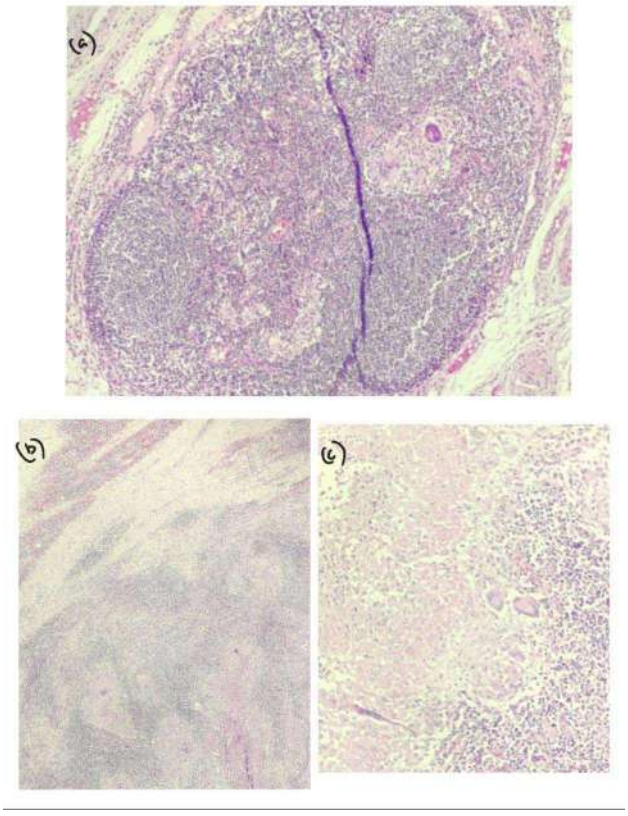

Figure 3. **a)** Well defined epithelioid granulomas. **b)** Numerous epithelioid granulomas with extensive areas of necrosis. **c)** Magnified granuloma showing multinucleated giant cells.

Discussion

An Italian anatomist Benevenni first described a mesenteric cyst while performing an autopsy on an 8- year old boy in 1507 [2]. In 1842, Rokitansky published the first accurate description of a chylous mesenteric cyst, and in 1880, Tillaux performed the first successful surgery for a mesenteric cystic mass.[2] Mesenteric cysts are a rare surgical condition that causes between one and three million hospital admissions each year [3].

Any cyst in the mesentery is considered a mesenteric cyst. The retroperitoneum, which has its own endothelium or mesothelium cell lining, may or may not contain it. From the duodenum to the rectum, mesentery cysts can occur anywhere in the digestive tract. In a review series of 162 patients, 60% of mesenteric cysts were found in the small bowel mesentery, 24% in the large bowel mesentery, and 14.5% in the retroperitoneum [4]. Mesenteric cysts can be single or multiple, unilocular or multilocular, and they may contain fluid that is infected, hemorrhagic, serous or chylous. They can go in size from a couple of millimeters to few cm in measurement, notwithstanding, on occasion might be enormous to such an extent that it might mimic ascites secondary to abdominal tuberculosis [5].

Although the exact cause of the mesenteric cyst has not been determined, infection, trauma and neoplasm are thought to be contributing factors, which does not allow lymph nodes to communicate with the lymphatic and vascular system [6]. Patients of any age may develop a mesenteric cyst. Roughly 33% of mesenteric cyst cases happen in children younger than 15 years. The cyst may manifest as an acute abdomen, a non-specific abdominal feature, or an incidental finding [7]. Pain, nausea and vomiting, constipation, and diarrhea, among other non- specific symptoms, are the most common. Up to 61% of patients an abdominal mass is palpable [7].

Mesenteric cyst needs to be assessed with thorough history, clinical assessment, blood examination and radiological investigations to arrive at a diagnosis. The diagnosis is confirmed on laparotomy and affirmed with histopathology [8]. In order to avoid a malignant transformation, complications, or recurrences, surgical excision is the preferred treatment. Laparoscopy should be the preferred method, but an intestinal loop resection along with “en bloc” resection of cyst may be required if the lesion cannot be safely enucleated [9].

Conclusion

On the other hand, tuberculous mesenteric cysts typically are multiple or have multiple locations and are associated with mesenteric lymphadenopathy. Due to their rarity, these mesenteric cysts are difficult to diagnose clinically, but prompt surgical excision and histopathological diagnosis will warrant the patient to necessary Anti Tubercular treatment [5].

Conflicts of interest

The authors declares that they do not have conflict of interest.

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CASE REPORT

Primary lymphoma of a cervix - a devil in disguise

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Abstract

Primary Lymphoma of the female genital tract a rare disease. Primary cervical lymphoma accounts for .008% of malignant cervical tumours. The symptoms and signs are nonspecific and very common. Papanicolaou cervical smear is not too much helpful in screening. Standard management protocol is not available for this disease. Here, we discussed a case of primary NHL of cervix presenting with abnormal bleeding per vaginum.

Keywords: primary cervical lymphoma, NHL -Non-Hodgkin's lymphoma, pap- smear, IHC – immunohistochemistry.

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Introduction

Lymphoma of the female genital tract is a rare disease [1]. Cervical involvement in non-Hodgkin's lymphoma (NHL) is common as a part of multiorgan disease but primary involvement of cervix is very uncommon. Because of rarity of disease, the clinical course, management and prognosis of primary gynaecological lymphoma is not well defined in literature. Here, we present a case of primary NHL of cervix presenting with abnormal bleeding per vaginum.

Case Report

A 47-year-old, P2 L2, diabetic and hypertensive women reported to Cancer Hospital and Research Institute in Gwalior after hysterectomy which was performed elsewhere. The histopathology of resected specimen revealed NHL of cervix.

On evaluation of old records, she had a history of irregular bleeding per vaginum for 6 months, which was not relieved with medical management. On preoperative examination, cervix was normal, uterus was bulky and retroflexed; bilateral fornices were normal. Her preoperative pap smear was normal and ultrasound showed a small intramural fibroid at fundus. She had no history of prolonged fever, weight loss, and night sweats. There was no history of similar condition in the family. She had no significant past and personal history.

She underwent total abdominal hysterectomy and bilateral salpingo-oophrectomy for fibroid uterus. Histopathology of surgical specimen revealed high-grade B cell lymphoma of cervix. This was confirmed on immunohistochemistry (IHC) as leucocyte common antigen (LCA) and CD20 showed strong and diffuse membranous positivity respectively while CK was negative in neoplastic cells.

Postoperative CT scan, one month after surgery, showed a large heterogenous mass in the uterine bed with infiltration of posterior wall of urinary bladder, rectum, sigmoid colon, and both distal ureters causing bilateral mild hydronephrosis. Her metastatic workup with CT thorax, bone marrow cytology, and peripheral smear were all normal. The disease was staged as primary cervical NHL stage II E using the Ann Arbor system. She was treated with 3 cycles of Rituximab, Cyclophosphamide, Doxorubicin, and Vincristine. Following 3 cycle of chemotherapy, she developed hydrocephalous with weakness of right upper and lower limb with neutropenia and deraigned renal function test. Despite treatment, her condition deteriorated and she expired after 16 weeks of primary surgery.

Discussion

Primary cervical lymphoma accounts for 0.008% of malignant cervical tumours [1]. The age of patient at diagnosis for cervical NHL ranges from 27 to 80 years (median 44years) [2]. The most frequent symptoms are pre or postmenopausal abnormal bleeding per vaginum, vaginal discharge, and abdominal pain. These symptoms are non-specific and common in gynaecological practice.

Physical examination reveals a diffusely enlarged or barrel-shaped cervix, often with absence of erosive or exophytic lesion. Therefore, it is difficult to differentiate NHL from benign lesions, like cervical fibroids, cervical inflammation, or Nabothian cysts clinically [3] (Figures 1 and 2).

Figure 1. Uterus is anteverted & anteflexed appears bulky with small 2cm size hypo echoic area at fundus represents intra mural fibroid. Cervix appears bulky without a definite growth or mass lesion. Peri-uterine fat planes with adjacent structures are grossly normal

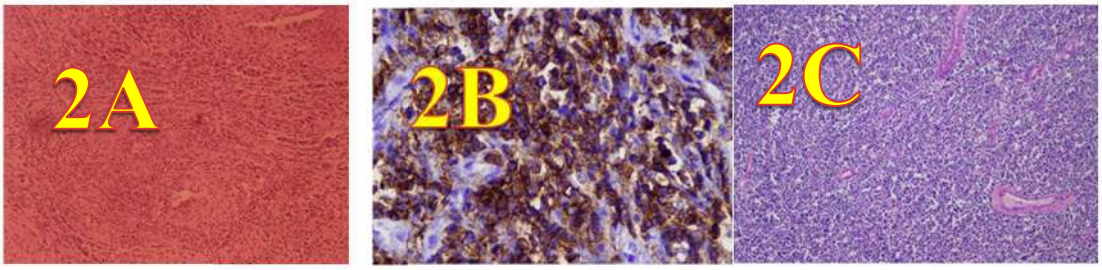

Figure 2. 2A: H&E (200x) - Large atypical lymphoid cells arranged in diffuse sheets. 2B & 2C: Immunohistochemistry (400x)- Tumour cells throwing diffusely positivity with LCA & CD20 respectively

Table 1. Interpretation of immunohistochemical stains in large lymphoid cells lymphoma.

CD45+(LCA)	Marker for leukocyte common antigen found in hematopoietic cells, thus indicating lymphoma.
S100+, PNL2+	Marker for melanoma.
Cytokeratin+	Marker for carcinoma.
CD20+	Marker for B-cell lymphoma.
CD10+, Bc12-, Ki67>99%	Immunohistochemical stain.
CD10+/-, Bc12+	Favours diffuse large B-cell lymphoma.
CD3+, CD20-	Marker for T-cell lymphoma.

Pap smear is not helpful in the screening and diagnosis of cervical lymphomas. As they usually arise from the cervical stroma rather than the mucosa, thus lacking the surface abnormalities. There is no gold standard among imaging techniques for diagnosing pelvic lymphoma. A high index of suspicion and use of ultrasound, MRI, and CT can suggest the diagnosis. PET CT may be performed for staging and metastatic assessment [4].

The importance of immunohistochemistry (IHC) in the diagnosis of primary malignant cervical lymphomas is well recognised (1). Currently, there is no specific IHC marker for lymphoma. Use of immunohistochemical stains, listed in Table 1, is necessary to establish a definite diagnosis when initial biopsy and usual stains are nonconclusive [3].

There is no consensus regarding the best treatment for Primary NHL of female genital tract. However, lymphomas are considered sensitive to chemotherapy and radiotherapy [4]. Chemotherapy regimen with R-CHOP is usually employed for lymphoma [2].

Case series reported that in most cases the management also includes surgery and/or radiation therapy. However combination of surgery and radiation therapy did not confer any survival benefit in most of cases. The role of surgery to improve overall survival is still unknown [1,3,5].

The prognosis may be excellent if the cervical lymphoma is diagnosed and treated correctly in an early stage. The 5-year survival rates have been reported to be 89% in early stage and 20% in II E-1V stage cases [1].

Conclusion

Primary cervical lymphoma is an uncommon disease that provides clinicians a diagnostic challenge. The diagnosis is often delayed due to non-specific clinical presentation and low index of suspicion. This condition has to be suspected in women with abnormal bleeding per vaginum, a suspicious cervix, and a normal Pap smear test. It is essential that the clinicians, radiologists, and pathologists have awareness for this rare disease.

Conflicts of interest

The author declares that they do not have conflict of interest.

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